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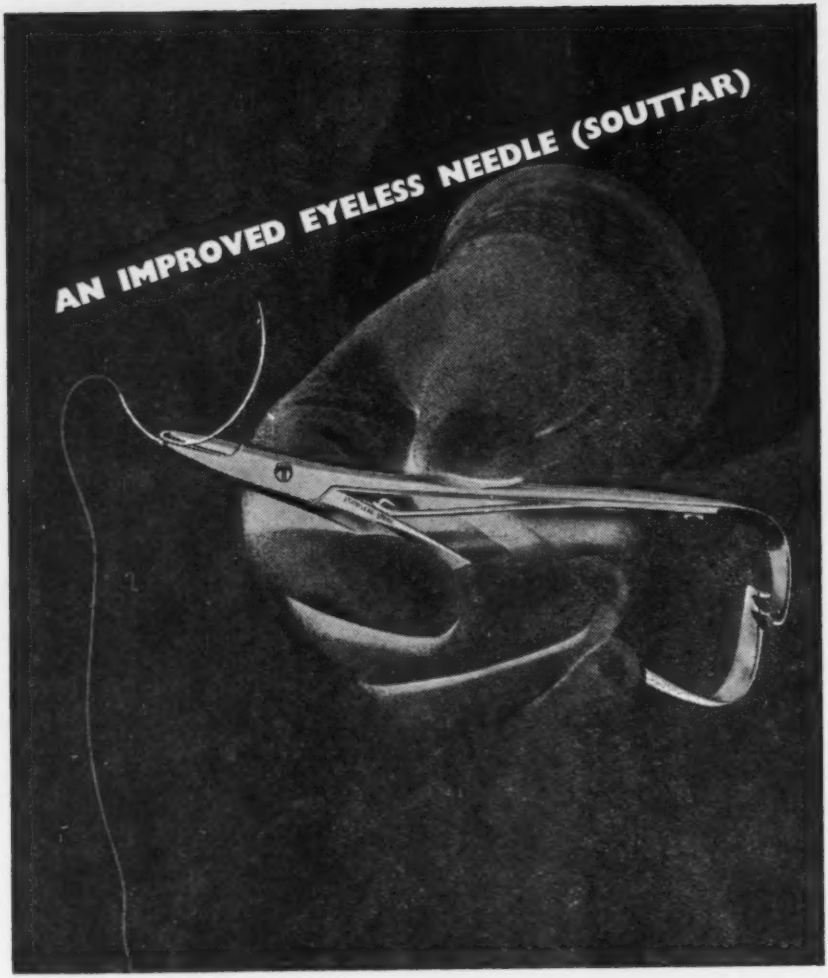

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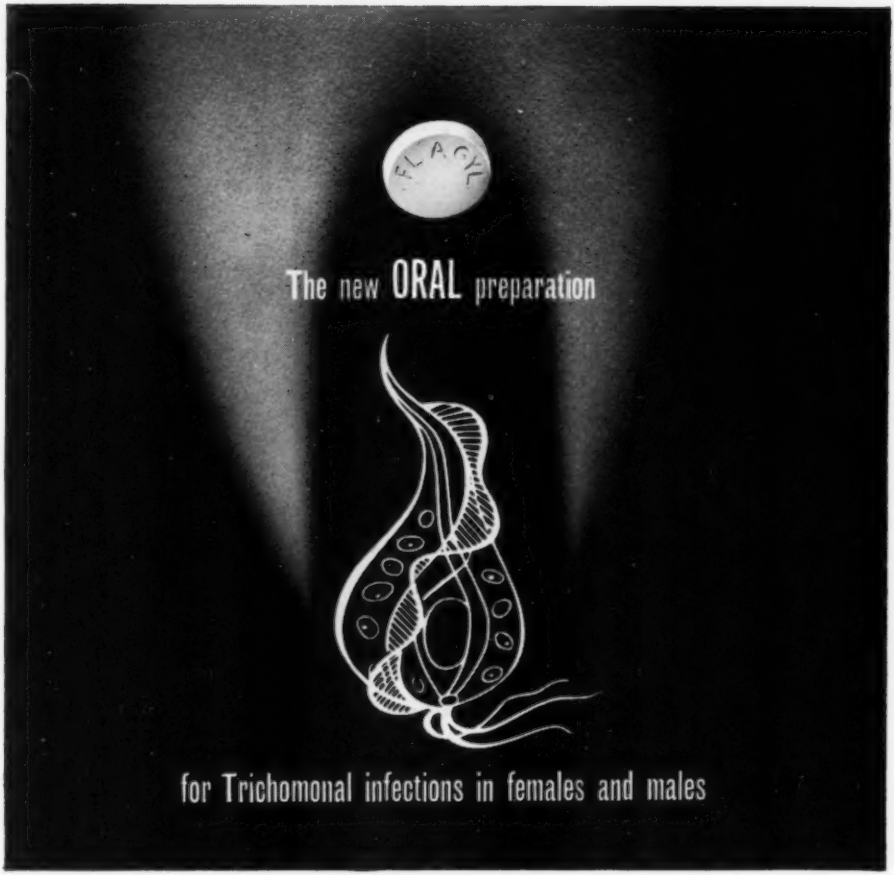

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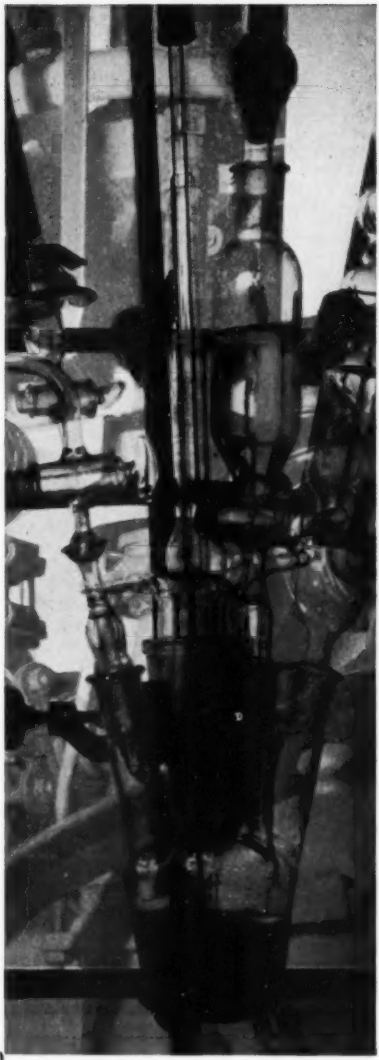

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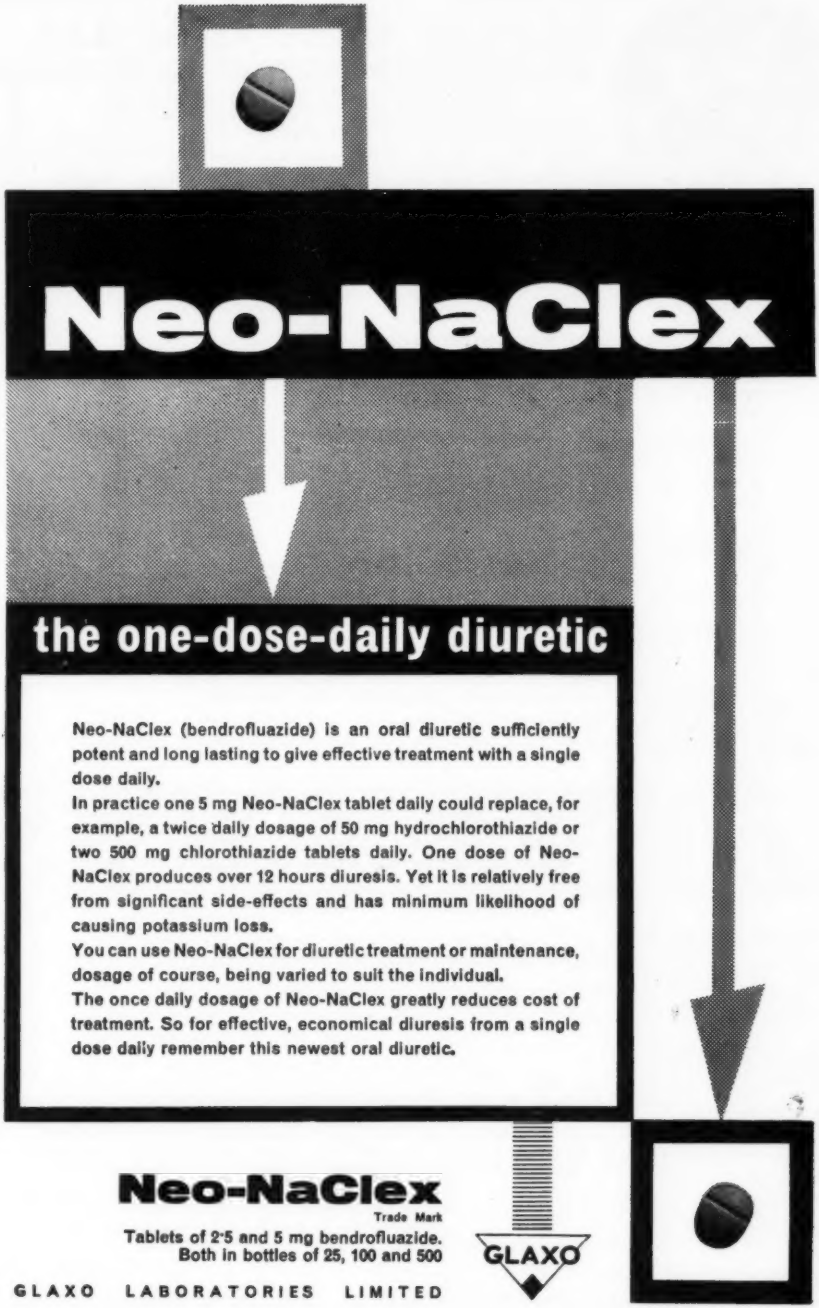
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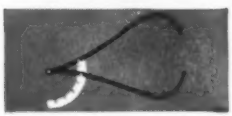

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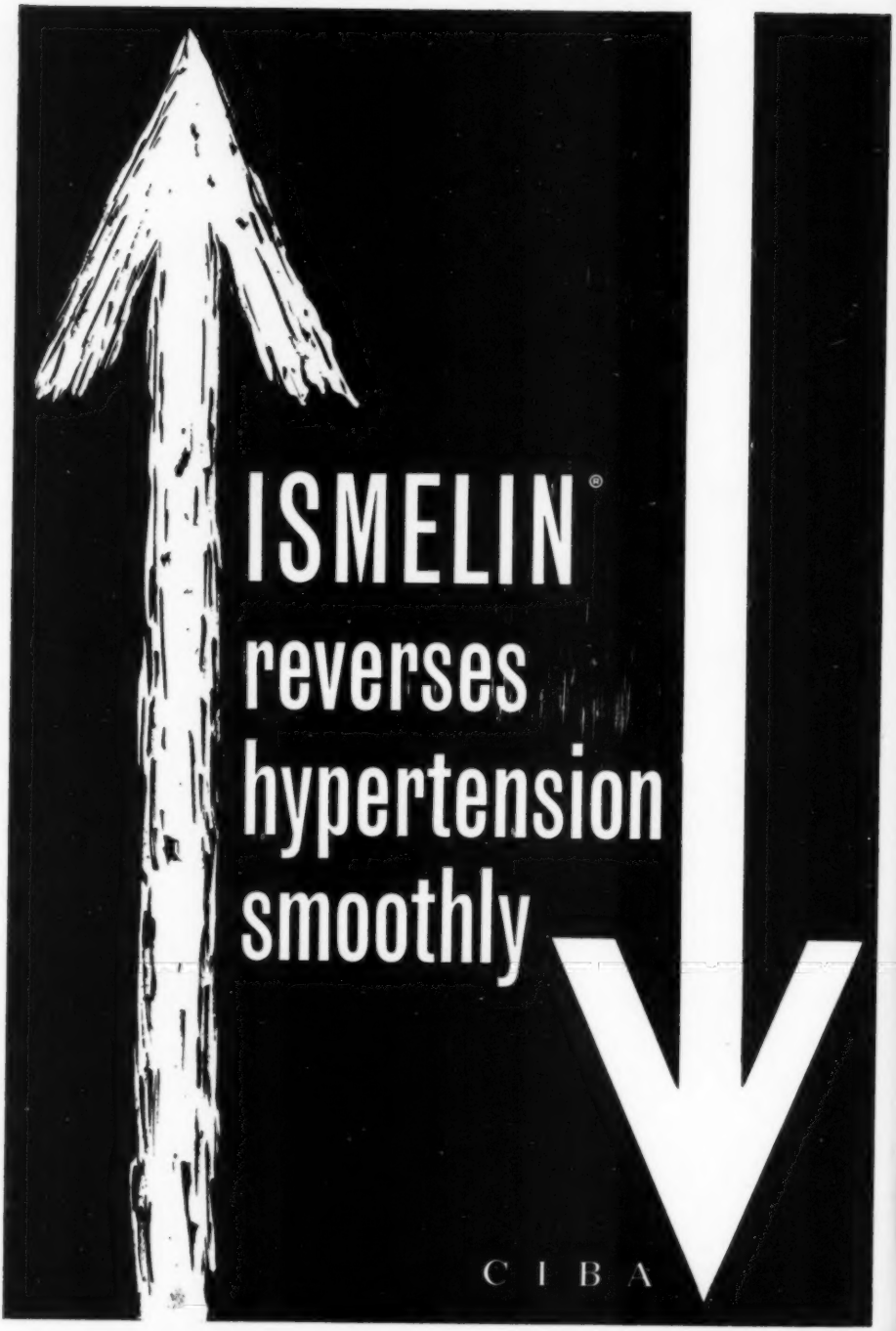
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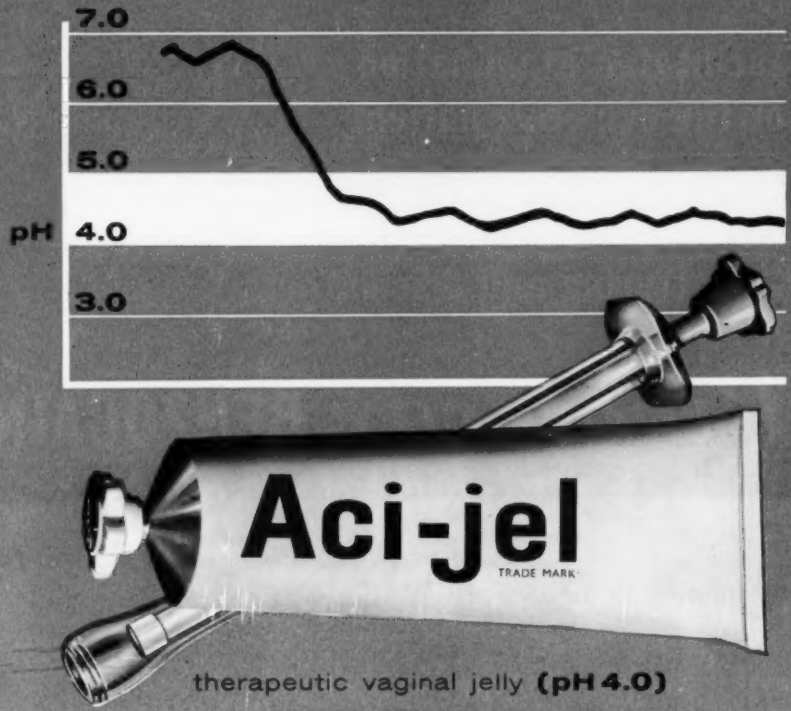

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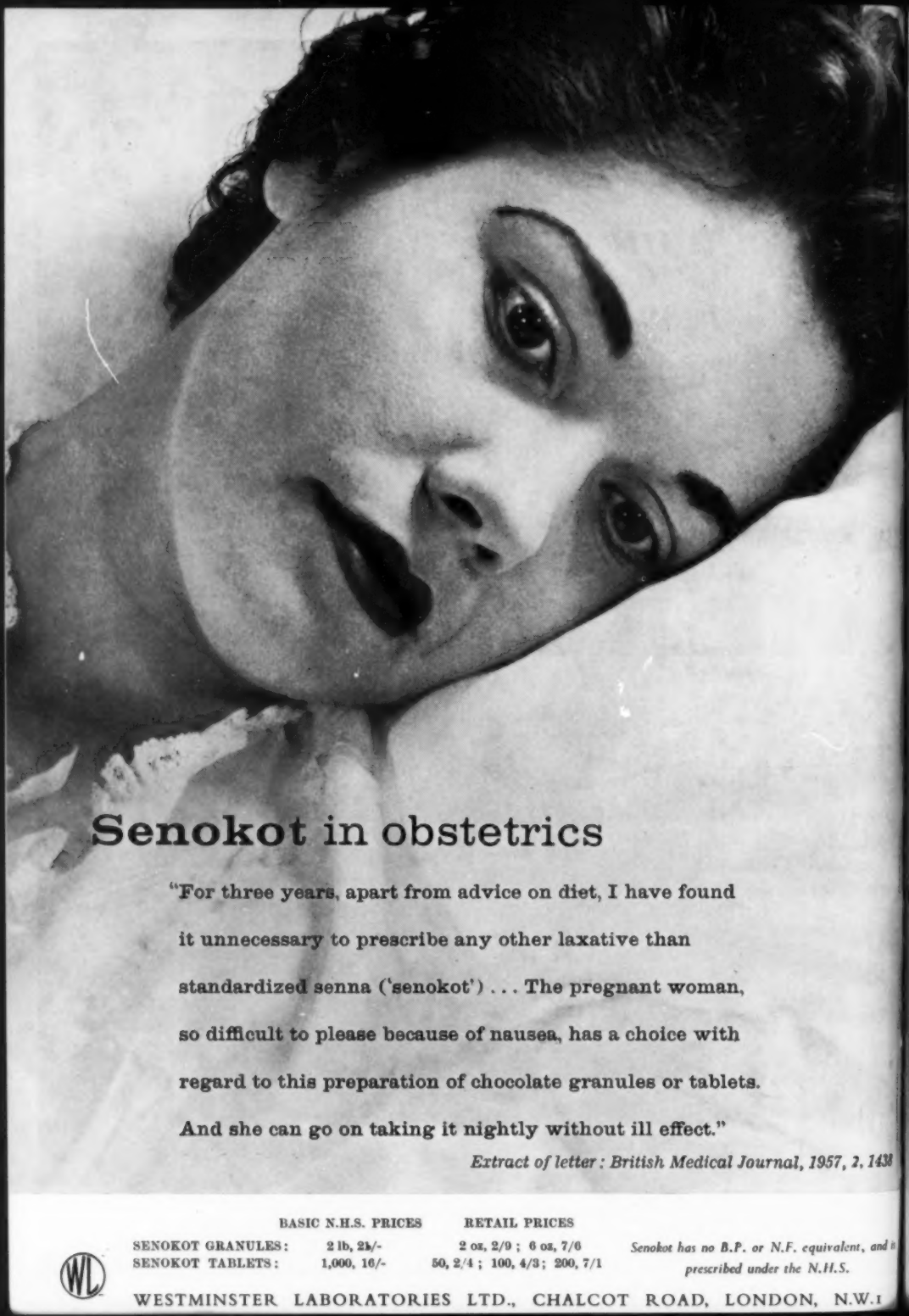

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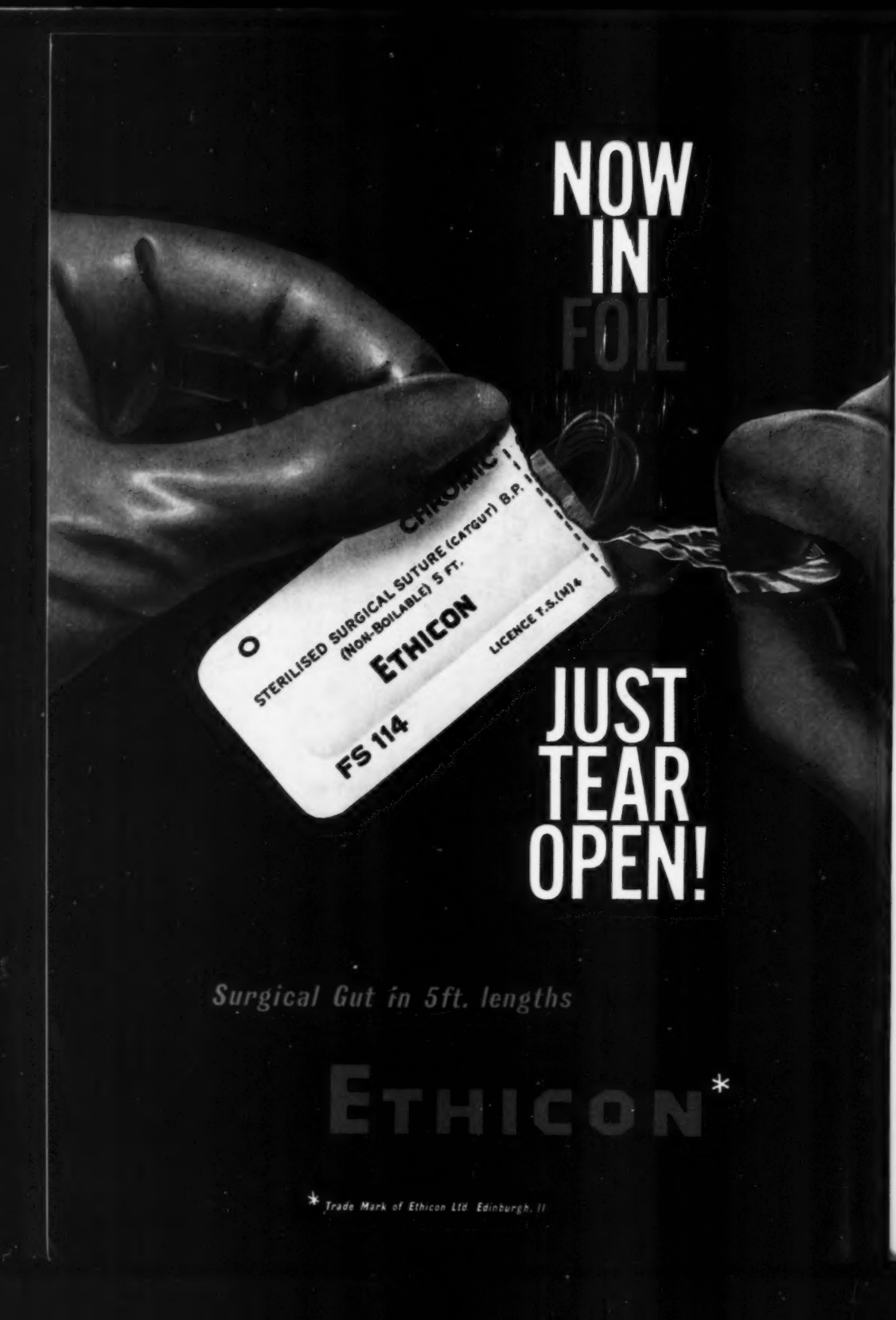
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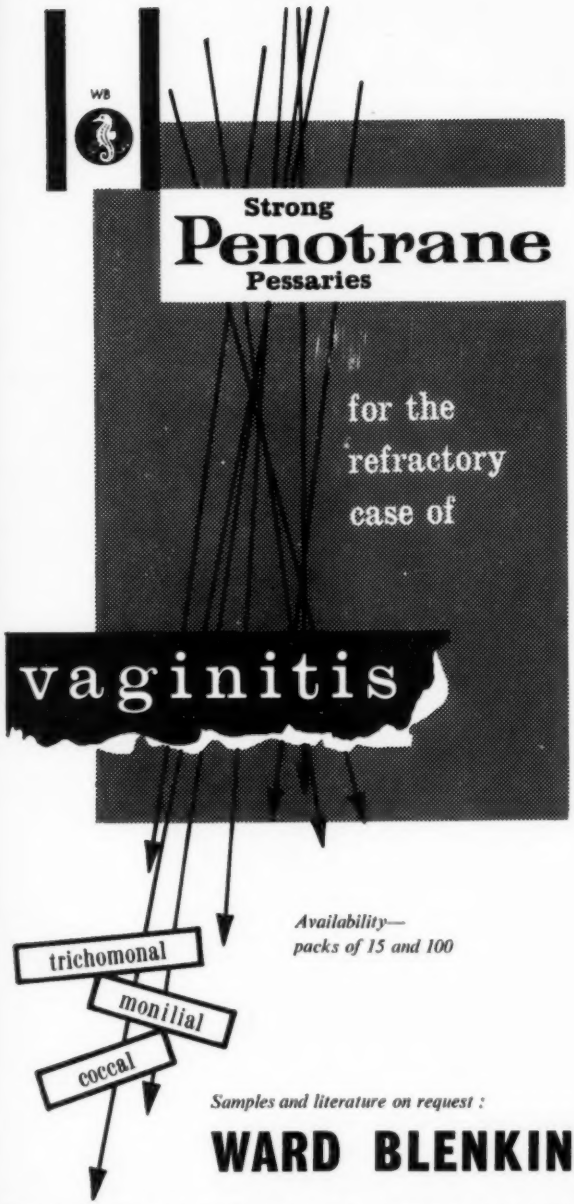

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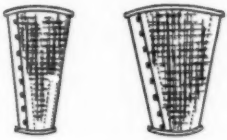

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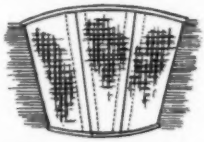

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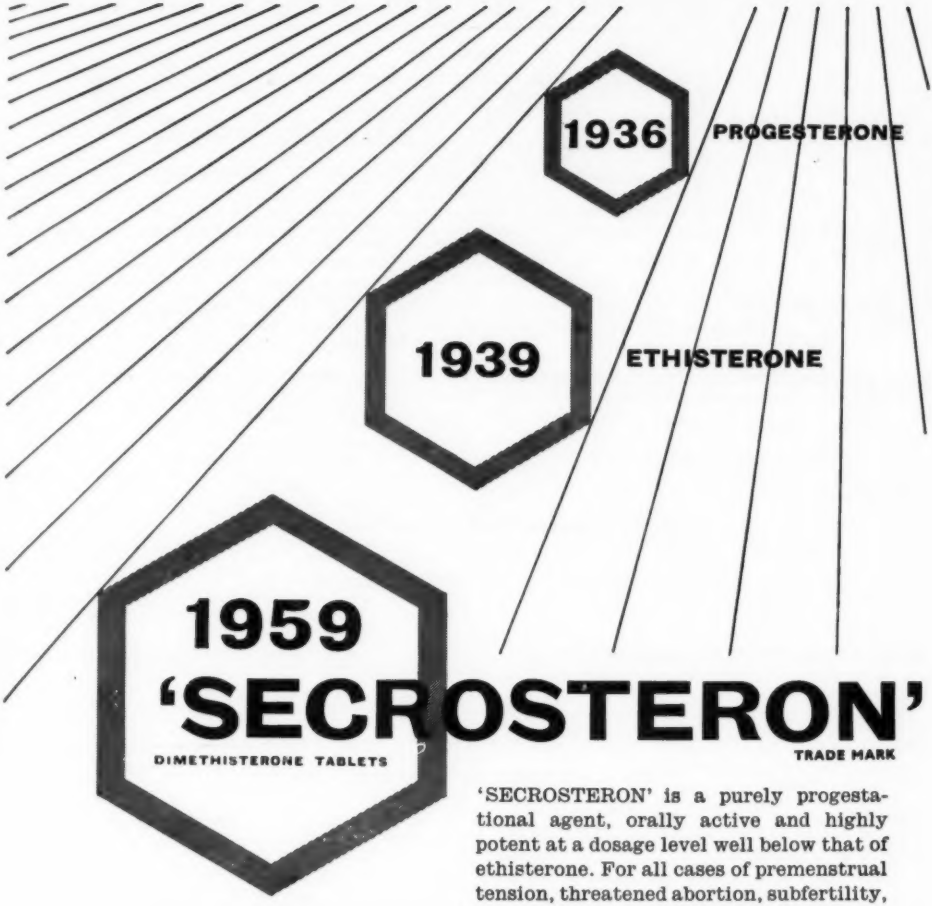

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THE ROLE OF THE POSTERIOR PITUITARY ANTIDIURETIC HORMONE IN TOXAEMIA OF PREGNANCY

BY

M. LINDSAY PATERSON, B.Sc., M.D., M.R.C.O.G.
Lecturer in the Regius Department of Midwifery
University of Glasgow

MR. President, Ladies and Gentlemen, I am extremely honoured to have this opportunity to deliver a William Blair-Bell Memorial Lecture. The subject of today's lecture is possibly a particularly suitable one to the occasion in that the late William Blair-Bell introduced the use of posterior pituitary extract to obstetrics in 1909 and amongst his other published works are several papers dealing with various aspects of pituitary function.

Dr. Scott in his lecture discussed pre-eclamptic toxaemia as a condition of hyperplacentosis and it is fitting that the present lecture should approach this disease from an entirely different viewpoint.

Before proceeding further I would like to express my thanks to Professor Ian Donald and Dr. A. D. T. Govan for their encouragement and assistance in the work on which this paper was founded. I must also acknowledge my indebtedness to the Leverhulme Fund of the Royal College of Obstetricians and Gynaecologists.

The aetiology of the toxaemias of pregnancy is a very complex subject and the more one reads the more baffled one becomes and the more glaring the contradictions appear. There seems general agreement that hormonal influence plays a considerable part in the aetiology, but there is no agreement whatsoever as to which endocrine gland, far less as to which hormone is involved. This is the only excuse I will offer for possibly making the question seem more complex and contradictory.

Of the three clinical facets which make up toxaemia of pregnancy, hypertension, albuminuria and oedema, the oedema, originally occult but later manifest, is generally the earliest to appear. It has been stated that of all patients who show an abnormal weight gain in pregnancy some third will later develop pre-eclamptic toxaemia and Hamlin (1952) by treating excessive gain in weight whenever it appeared was able, almost, to abolish pre-eclamptic toxaemia and eclampsia from his antenatal practice. This excess weight gain is due to retained water and amongst the possible causes for retention of water is excessive activity of the antidiuretic hormone of the posterior pituitary gland. It is the results of an investigation into the occurrence and titre of antidiuretic hormone in toxaemia of pregnancy that I wish to present to you.

There is nothing new in the suggestion that the posterior pituitary gland has a part to play in the aetiology of pre-eclamptic toxaemia. This was first suggested by Hofbauer in 1918 when he postulated that pregnancy toxaemia was a sequel to disturbance of the normal neurohypophyseal-adrenal equilibrium. As Hofbauer could produce no experimental work to support this theory nothing more was heard of it until 1927 when it was taken up by Rossenbeck and by Küstner. The proofs advanced by these authors are however no longer fully acceptable and it is to Anselmino, Hoffmann and Kennedy (1932) that the credit belongs for demonstrating pressor and antidiuretic activities identical to these of the posterior pituitary gland in blood

of eclamptic and pre-eclamptic patients. These workers further claimed that quantitative estimations ran parallel with the severity of the symptoms.

The next support for the posterior pituitary theory was anatomical and histological. Cushing (1933) in the course of an anatomical investigation into the function and activity of the neurohypophysis demonstrated that in fatal cases of eclampsia there was a massive basophilia of the pars nervosa. The following year the same worker extended these observations and reported the findings in nine fatal cases of eclampsia. It appeared that the basophilia was related to the degree of hypertension. Ahlström (1935) who continued this work was unable to confirm entirely the findings of Cushing but concluded that there was some relationship between the posterior pituitary gland and the toxaemias of pregnancy. If Ahlstrom's work is re-assessed in the light of the known fact that the pressor and antidiuretic hormones of the posterior pituitary gland are one and the same. it will be noted that, in fact, the findings are compatible in that these cases which Ahlström felt did not agree with the work and the conclusions of Cushing are the cases where hypertension was slight but oedema was marked as was the basophilia. So far the evidence has all been in support of the posterior pituitary theory, but in 1934 de Wesselow and Griffiths and in 1935 Hurwitz and Bullock were unable to confirm the existence of any posterior pituitary pressor substance in the blood of the pre-eclamptic. For the next ten years the reports are almost evenly divided between support for and rejection of the occurrence of posterior pituitary activity in pre-eclampsia. Then in 1940 the position was further complicated by Krieger and Kilvington who claimed that the antidiuretic hormone could be extracted from the urine of normal pregnant and even non-pregnant women as well as that of toxaemic patients. In 1946 these authors reviewed their work and claimed that significant amounts were only found in the urine from toxaemic patients but in 1951 Krieger, Butler and Kilvington reported that certain strains of *Escherichia coli* produced an antidiuretic substance and this led them to state that after due consideration their previous results could possibly have been due to bacterial contamination of the urine. They concluded that it was unlikely that antidiuretic substances of pituitary origin could be regularly detected in the urine of toxaemic patients and with this conclusion Willson, Carrington, Hadd and Boutwell (1954) were in agreement. More recently in 1954 I published a preliminary paper on this subject and in 1957 Hawker working in Edinburgh reported the presence of posterior pituitary antidiuretic hormone in the blood of toxaemic pregnant women.

Despite the controversy that exists regarding the presence or absence of posterior pituitary activity in pre-eclamptic toxaemia it has long been known that these patients exhibit a marked sensitivity to posterior pituitary extract. This has been shown by Dieckmann and Michel (1937), Schockaert and Lambillon (1937), de Valera and Kellar (1938) and this increased sensitivity has been variously attributed to the action of the gonadotrophic hormones either of chorionic or pituitary origin (Byrom, 1938; Browne, 1946; Govan and Mukherjee, 1950).

In view of the wide divergence of opinion which I have briefly reviewed I decided to re-investigate the place of the antidiuretic hormone of the posterior pituitary gland in the causation of the acute toxaemias of pregnancy, using the more up-to-date methods of paper chromatography allied to the more sensitive methods of assay which are now available.

As you will know the posterior pituitary hormones are secretions of the hypothalamic nuclei from where they migrate along the axons of the supra-optico-hypophyseal tract to be stored in the posterior pituitary lobe. In man, however, only a very small fraction of the total hormone stored can be recovered from the hypothalamus and some 99 per cent of the total storage is in the posterior pituitary gland. Two hormones can be differentiated, the one the pressor or antidiuretic hormone with which we are concerned, the other the oxytocic hormone. These hormones exist side by side and in the posterior pituitary gland the ratio of pressor to oxytocic approaches unity. Both hormones are liberated in response to stimuli of which variation of the osmotic pressure of the blood and suckling are the more physiological. Other

stimuli known to produce liberation of the posterior pituitary hormones in man include emotional stress, fainting, shock and severe haemorrhage, certain drugs such as Pethidine, anaesthetic agents and nicotine and in response to these various stimuli the posterior pituitary gland secretes the two hormones in varying proportion. The pure hormones have recently been isolated by Du Vigneaud and his co-workers (1953) and they have shown that vasopressin is a peptide with eight constituent amino-acids, seven of which are constant, the eighth varying as to the animal source of the pituitary gland. However secreted, antidiuretic hormone circulates in the blood stream and acts on the kidney causing inhibition of water diuresis, without change in the blood flow through the kidney. The quantity of anti-diuretic hormone which produces this result is very small. In a dog weighing 10 to 15 kg. deprived of its posterior pituitary lobe the intravenous injection of 1 to 5 thousandths of a unit of antidiuretic hormone per hour will inhibit water diuresis. It is now accepted that the action of the extract on the kidney is to cause the re-absorption of water by the tubules without great change in excretion of other urinary constituents. Antidiuretic hormone is normally destroyed by the liver although some hormone may be excreted in the urine. It has also been suggested that cortisone may play a part in the destruction.

Extraction and Identification of the Antidiuretic Hormone

Arneil and Wilson (1953) and Valeri, Zacco and Perrini (1953) had suggested that the anti-diuretic hormone could be isolated by two-dimensional paper chromatography and this was the method employed. The first diagram is an illustration of the method. If a mixture of amino-acids and polypeptides is applied to a sheet of filter paper as a spot and a solvent not miscible with water allowed to creep slowly along the filter paper past the spot then the amino-acids or polypeptides are drawn along at definite speeds behind the moving solvent front and thus arrange themselves in a characteristic order. In the diagram it will be seen that this spot contains

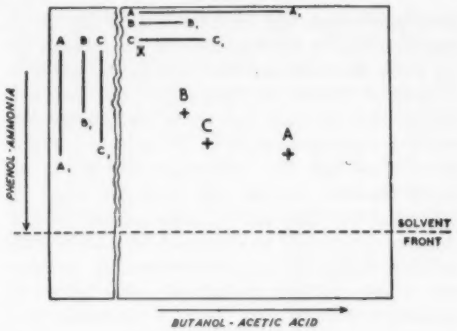

Diagram I

To illustrate method of separation and identification of amino-acids in a mixture, by means of two-dimensional chromatography.
X—Point of application of unknown mixture.
A–A,—Distance selected amino-acid will run in either phenolammonia or butanol acetic acid—hence
A, B and C are the ultimate positions on the two-dimensional chromatogram.

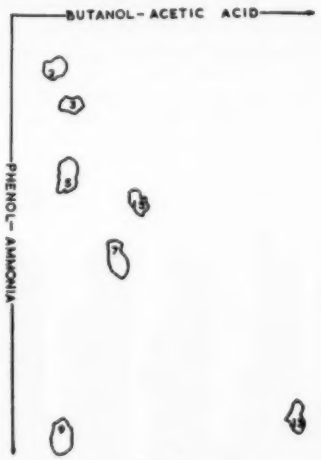

Fig. 1

Chromatogram developed from normal pregnant urine. Note absence of any substance in the characteristic position of the antidiuretic hormone.

Key to all Chromatograms

1. Cystine	6. Threonine	11. Valine
2. Aspartic acid	7. Alanine	12. Phenylalanine
3. Glutamic acid	8. Lysine	13. Leucine
4. Serine	9. Arginine	14. Tyrosine
5. Glycine	10. Proline	15. Histidine

three substances and that these after the paper has been run in the first solvent have taken up the three positions marked one. If the paper is then dried, turned at right angles and run in a second solvent then the three substances will travel a varying distance in the second solvent. By this method two substances which run an equal distance in the first solvent may be separated by the use of the second and a chromatogram will be obtained on which, after staining, either by direct mensuration or later by experience the individual spots may be identified. Figure 1 is such a chromatogram developed from normal pregnant urine and shows a fairly typical amino-acid pattern as seen in the pregnant. It was soon found, that almost constantly present in the urine of toxaemic pregnant patients was a substance which took up a characteristic position on the two-dimensional chromatogram and this substance is shown in Figure 2. The only difference between chromatograms developed from the urine from normal pregnant women and chromatograms developed from urine of toxaemia of pregnancy was the presence of this substance in its characteristic position. To all other intents and purposes the chromatograms were identical and no variation in the amino-acid output was detected either in quantity or in the presence of unusual or abnormal amino-acids. It will be noted that this substance in the urine from toxaemia takes up a position at the end of the first solvent run and is virtually unmoved by the second solvent. This characteristic forms a useful method for the isolation of the substance in greater quantity for further investigation. If instead of applying the mixture as a spot it was instead applied as a line along the length of a sheet of filter paper then by running in the first solvent the substance under investigation would run to the solvent front. The paper was then dried and this time turned through 180 degrees. The other amino-acids present were then moved on in the second solvent while the substance under investigation was virtually unmoved and could later be extracted from the area of the first solvent front. By this means and the running of multiple papers supplies were obtained for further investigation of the chemical structure and for assay in animals.

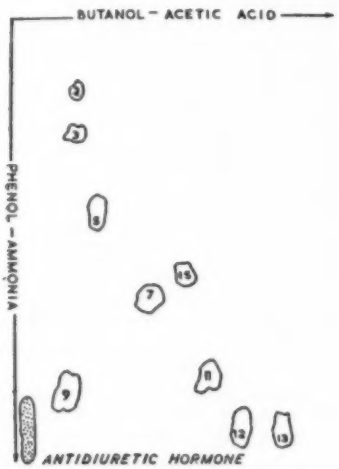

FIG. 2

Chromatogram developed from urine of pre-eclamptic patient.
Note presence of characteristically situated "spot". This is in fact the antidiuretic hormone.

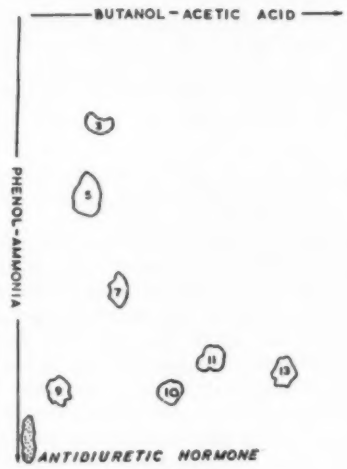

FIG. 3

Chromatogram developed from commercial pituitary extract.
To show the presence of the antidiuretic hormone in characteristic position.

If now instead of using urine, commercial posterior pituitary extracts were employed for the development of chromatograms then it was found that in each and every posterior pituitary extract a substance in the characteristic position on the chromatogram was present. Figure 3 is a chromatogram developed from one of these extracts.

It now became necessary to discover whether the activity of commercial pituitary extract was in any way associated with this substance and to do this commercial posterior pituitary extract was separated chromatographically into eight separate portions. It was then found that only that portion which contained the substance under investigation and no other portion demonstrated antidiuretic activity. It therefore seemed possible that this substance was associated with posterior pituitary activity.

The opportunity was taken to obtain human posterior pituitary glands from patients who had died in the Glasgow Royal Maternity and Women's Hospital. These glands were extracted by the method laid down in the *British Pharmacopoeia*, 1953 for the preparation of posterior pituitary extract and the extract subjected to chromatography. Figure 4 is a chromatogram developed from one of these extracts and it will be noted that the characteristic substance is present. Once again when these extracts were chromatographically separated and submitted to assay it was found that only in that portion of the extract which contained the substance under investigation was activity present.

I now went back to extracts obtained from the blood or urine of eclamptic and pre-eclamptic patients and submitted these extracts to assay and found that where this substance was present then antidiuretic activity could be demonstrated.

Antidiuretic assay is carried out in the hydrated rat whose kidneys are subjected to maximal secretion. Alcohol is used as an anaesthetic and also to depress endogenous antidiuretic hormone output (Ames and Van Dyke, 1952). Under these conditions the intravenous injection of antidiuretic hormone resulting in diminution of the urine flow is almost a specific test for posterior pituitary antidiuretic hormone and an accurate measure of quantity. Figure 5 is a normogram of the antidiuretic

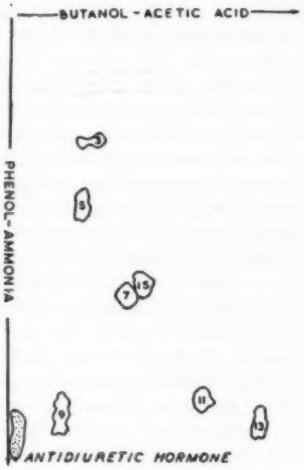

FIG. 4

Chromatogram developed from extract of human posterior pituitary gland.
Note characteristically situated antidiuretic hormone.

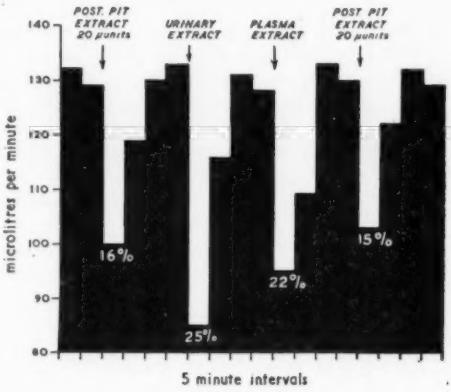

FIG. 5

Depression of urinary output in the hydrated rat (Ames and Van Dyke, 1952), in response to antidiuretic hormone extracted from the urine and plasma of pre-eclamptic patients.

assay of this material extracted from the urine and plasma of a pre-eclamptic patient and it will be noted that the urine flow of the rat preparation is diminished by the intravenous injection of this substance. For comparison purposes the same rat preparation was given a small dose of commercial pituitary extract and once again you will note the diminution in the urine flow.

It has long been known that the antidiuretic activity of posterior pituitary extract can be destroyed by incubation with sodium thioglycolate and it is confirmatory that incubation with this substance completely abolished the antidiuretic activity of the substance under investigation.

As further identification of the material under test, supplies obtained from (1) urine of pre-eclamptic patients, (2) blood of pre-eclamptic patients, (3) commercial pituitary extracts, and (4) the human pituitary, were all submitted to acid hydrolysis. After reduction of the acidity by evaporation the hydrolysates were developed as two-dimensional chromatograms. The amino-acid pattern in each case was identical. Figure 6 is the chromatogram of a hydrolysate developed from pre-eclamptic urine, while Figure 7 is a chromatogram of a hydrolysate developed from human pituitary extract. It will be noted that these chromatograms are identical and that each contains the same 14 amino-acids. I have already said that pure vasopressin has been isolated as an octopeptide, an eight amino-acid structure, but it is noteworthy that the fourteen amino-acids at present described are in fact the same fourteen amino-acids as a high potency preparation of vasopressin which Turner *et al.* (1951) found as one of their intermediate stages in the preparation of pure vasopressin and that all the amino-acids contained in pure vasopressin are also contained in the present substance. It would appear therefore that this is in fact an impure sample of the posterior pituitary hormone possibly linked to some other peptide or contaminated by some other peptide. Table I gives the comparison between the various amino-acid analyses and shows the relationship of the present substance to pure vasopressin.

It appeared from the foregoing that this substance, isolated in a characteristic position on the chromatogram, was in fact a polypeptide

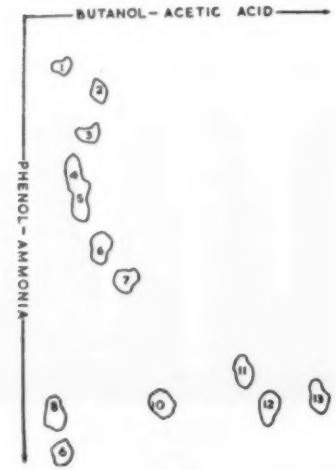

FIG. 6

Chromatogram developed from acid hydrolysate of antidiuretic hormone derived from pre-eclamptic urine. Compare amino-acids present with Figure 7.

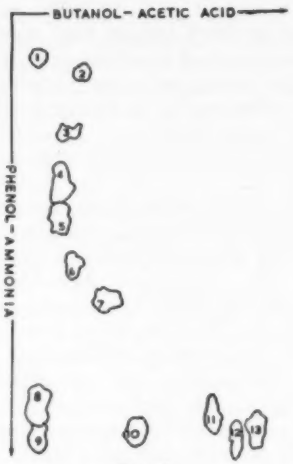

FIG. 7

Chromatogram developed from acid hydrolysate of antidiuretic hormone derived from human posterior pituitary gland.

For comparison with Figure 6.

TABLE I

Comparative Amino-acid Analysis of Present Substance and Pure Vasopressin

Amino-acids	Present Series	Turner *et al.* (1951)		Vasopressin Du Vigneaud *et al.* (1953)	
		Fraction 1	Fraction 6	Beef	Hogg
Alanine	+	+			
Arginine	+	+	+	+	
Aspartic acid	+	+	+	+	+
Cystine	+	+	+	+	+
Glutamic acid	+	+	+	+	+
Glycine	+	+	+	+	+
Leucine	+	+			
Lysine	+	+			+
Phenylalanine	+	+	+	+	+
Proline	+	+	+	+	+
Serine	+	+			
Threonine	+	+			
Tyrosine	?(+)*	+	+	+	+
Valine	+	+			

* Tyrosine was not found in all the hydrolysates. This is explained by the partial or complete destruction of tyrosine by acid hydrolysis.

and that this polypeptide was also an active principle of the posterior pituitary gland. As further proof of this several experiments were carried out. The first entailed the examination of the blood and urine of three cases of diabetes insipidus of central origin both before and after treatment. It is noteworthy that in neither the bloods nor the urines of these patients before treatment was it possible to demonstrate the present substance, but that in both the blood and urine of these patients after treatment by substitution therapy with posterior pituitary extract the substance was invariably found when the patient was in a state of clinical cure; while the patient was in a state of constant diuresis when the substance was absent.

Two further experiments will be described here. It is known that the antidiuretic activity of nicotine is mediated through the posterior pituitary gland. The following experiment was carried out. Non-smokers only were selected. A sample of urine was obtained and thereafter a litre of water drunk. This was done so that the subjects would be in a state of diuresis and any naturally occurring antidiuretic hormone would be overcome, Half an hour after drinking the litre of water a second specimen of urine was obtained and the volunteers were then asked to smoke a cigarette inhaling as much as was possible. Six commenced this experiment but after the inhalation of the cigarette one vomited and was therefore excused further participation. The remaining five passed a further specimen of urine at the end of an hour and the experiment then terminated. Analysis of the urine both in the normal state and after ingestion of a litre of water showed no antidiuretic activity whatsoever but after the inhalation of the cigarette, a well-marked antidiuresis appeared, the urine demonstrated considerable antidiuretic activity and in each case the present substance could be demonstrated.

A similar experiment was undertaken but instead of smoking a cigarette, five units of pituitary extract were injected intramuscularly. The results were in all respects similar. Prior to the injection of the pituitary extract the present substance could not be demonstrated. After injection of pituitary extract antidiuresis occurred, antidiuretic activity could be assayed in the urine and the same polypeptide was in each and every case demonstrable. It is therefore held that the substance under discussion is in fact an active principle of the posterior

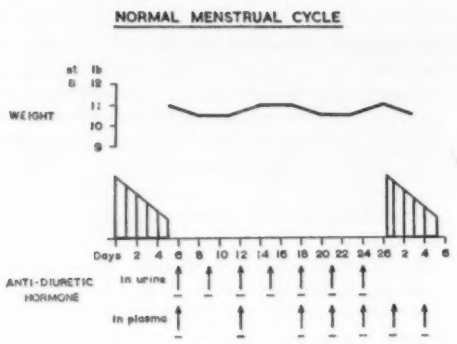

FIG. 8

Normal menstrual cycle.
Note absence of antidiuretic hormone from urine and plasma throughout cycle. Weight remains stationary.

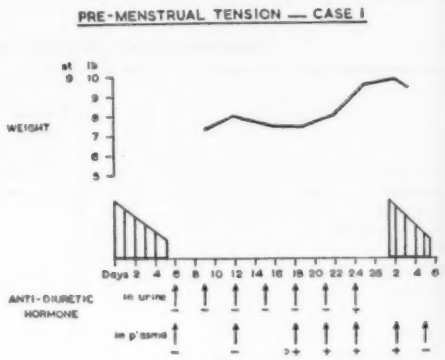

FIG. 9

Pre-menstrual tension. Case No. 1.
Note that appearance of antidiuretic hormone in plasma precedes weight gain and also precedes appearance of antidiuretic hormone in urine.

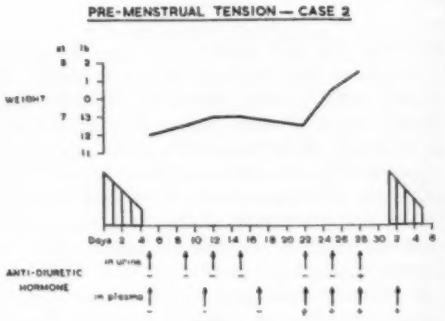

FIG. 10

Pre-menstrual tension. Case No. 2.
Appearance of antidiuretic hormone and weight gain coincide but both precede appearance of antidiuretic hormone in urine.

pituitary gland and with this established I would like now to go on and describe the findings in the normal pregnant, the pre-eclamptic and the eclamptic patient.

CLINICAL RESULTS

Before proceeding to any study of the occurrence or titre of antidiuretic hormone in pregnancy it was necessary to establish whether this substance was found in the non-pregnant female during the reproductive period of life. It has been suggested that pre-menstrual tension could be due to an excess of antidiuretic hormone in the second half of the cycle and several authors (Robinson and Farr, 1940; Lloyd and Lobotsky, 1950) had reported findings to support this. For this reason six healthy, normotensive volunteers were followed through a menstrual cycle, as were four who admitted to the symptoms of pre-menstrual tension. Figure 8 reports the serial investigation of the blood and urinary status as regards antidiuretic hormone during a normal menstrual cycle. It will be noted that this patient exhibited no evidence whatsoever of weight gain during the second half of the cycle and it will also be seen that antidiuretic hormone was not detected at any time in either the urine or plasma. For comparison, see Figures 9 and 10. Here it will be noted that antidiuretic hormone was detected in the plasma in the second half of the menstrual cycle and that the appearance of this substance in the plasma preceded its appearance in the urine. It will also be noted that the appearance of the antidiuretic hormone in the plasma coincided with or preceded in time the weight gain noted in the patients. These cases of pre-menstrual tension were the only occasions in

numerous investigations in which antidiuretic hormone could be detected in either the plasma or the urine of the normal non-pregnant female.

I next examined the urine of a group of normal pregnant patients. These ninety-six women had been admitted to hospital for some reason other than hypertensive toxaemia, essential hypertension or chronic nephritis in pregnancy. On clinical examination they proved to be normotensive, without oedema, and albumin was absent from the urine. They represented all periods of gestation and Table II gives the results

TABLE II

Urinary Findings in Non-Toxaemic Pregnancy

No. of Cases in Group	Duration of Pregnancy (Weeks)	Antidiuretic Hormone	
		Negative	Positive
20 ..	Less than 14	20	0
20 ..	14–28	20	0
30 ..	28–40	28	2
26 ..	40+	26	0
7 ..	3rd day } Post-	7	0
6 ..	5th day } partum	6	0
8 ..	7th day }	8	0

obtained. In the antenatal period it will be noted that antidiuretic hormone was only detected on two occasions and although both these patients were submitted to further investigation the results could not be confirmed. Whether these results were in error or whether confusion of specimens had arisen I am unable to say. The urine was also examined for antidiuretic activity in the immediate puerperium. This was done as Hawker (1952) has suggested that the onset of lactation and the titre of antidiuretic hormone were directly connected. In the patients examined I was unable on any occasion to detect evidence of antidiuretic hormone in the urine.

The results of the investigation of the blood of the normal pregnant group are shown in Table III. These patients were in the main the same group as those in whom the urinary findings have just been reported. It will be noted that in the antenatal period antidiuretic hormone was detected in the plasma on five occasions and

TABLE III

Plasma Findings in Non-Toxaemic Pregnancy

Duration of Pregnancy (Weeks)	No. of Patients	Antidiuretic Hormone	
		Positive	Negative
0–14	7	0	7
14–28	11	0	11
28–40	23	3	20
40+	14	2	12
3rd day } Post-	5	2	3
5th day } partum	5	0	5

in each case these positive findings were confirmed. In none of these cases could the hormone be detected in the urine and no significant difference could be detected between the clinical picture of those patients whose plasma did contain antidiuretic hormone and those in whom assay was negative. In the cases with positive plasma results investigations were continued in the puerperium. In two of these five patients antidiuretic hormone was present in the plasma on the third day but by the fifth day was absent in all cases. In only one of the two patients in whom antidiuretic hormone was found in the urine did it prove possible to examine the plasma. In this case the plasma assay was negative and this result lends support to the conclusion that the finding was in error, as a positive urine has never in any other case been found in the presence of a negative plasma.

Very different findings were found in the next group investigated who were the pre-eclamptics. The criteria necessary to establish the diagnosis of pre-eclampsia were:

(1) That the patient be 28 or more weeks pregnant.

(2) That the blood pressure be 140/80 mm. of mercury or greater.

(3) That albuminuria, oedema or both be present.

The urine of 86 patients who satisfied these criteria was submitted to investigation. Table IV gives the results obtained and here the patients have been split up into groups according to the clinical estimate of the oedema present. Where

TABLE IV

Urinary Findings in Pre-eclamptic Toxaemia Related to the Degree of Oedema

Clinical Estimate of Oedema	No. of Cases Examined	Antidiuretic Hormone	
		Present	Absent
Marked	14	14	0
Moderate	64	63	1
Slight	6	2	4
Absent	2	0	2

oedema was marked antidiuretic hormone was present in the urine of all cases examined. Where oedema was moderate antidiuretic hormone was present in 63 of 64 cases examined, but where oedema was slight antidiuretic hormone was only present in two cases and absent in four, while, where oedema was absent, the antidiuretic hormone was not detected in the urine of the only two cases examined. Of the total of 86 patients examined, 79 showed the presence of the antidiuretic hormone in the urine, while 7 did not. Table V gives the clinical details of these cases where antidiuretic hormone was absent and affords further evidence of the correlation of the antidiuretic hormone with the estimate of the oedema.

Examination of the plasma was carried out in 53 of the cases whose urinary status was known. Table VI gives details of these cases, once again correlated to the clinical estimate of the oedema. A new column makes its appearance here under the heading "Presence of Antidiuretic Hormone" and that is the column labelled "Doubtful". The term "doubtful" implies that antidiuretic hormone could be detected on chromatography but that this finding could not be confirmed by bioassay. It will be noted that of the 53 plasmas examined 48 showed the presence of the hormone, 3 are classed as doubtful, while in 2 the hormone was absent and it will be further noted that the doubtful cases and particularly the 2 in which the hormone was absent were those in which oedema was least marked. Table VII is somewhat complicated, but is presented in an attempt to relate the estimate of the oedema, the presence of antidiuretic hormone in the urine and the presence of the same substance in the plasma. In no case of pre-eclampsia where antidiuretic hormone was detected in the plasma was the

TABLE VI

Plasma Findings in Pre-eclamptic Toxaemia Related to the Degree of Oedema

Clinical Estimate of Oedema	Number of Cases	Presence of Antidiuretic Hormone		
		Positive	Doubtful	Negative
Marked ..	11	11	0	0
Moderate ..	37	36	1	0
Slight ..	3	1	2	0
No oedema	2	0	0	2

TABLE V

Clinical Details of the Seven Pre-eclamptic Patients in Whose Urine no Antidiuretic Hormone was Found

Maturity Weeks	Blood Pressure mm. of Hg	Oedema	Albuminuria g./litre	Antidiuretic Hormone
40	170/100	Trace	½	Not detected
36	150/105	Trace	1	Not detected
39	145/ 85	Slight	0	Not detected
40+	150/ 90	Trace	1	Not detected
40	155/ 85	Nil	½	Not detected
37	210/120	Nil	2	Not detected
40+	150/ 90	Trace	0	Not detected

TABLE VII

The Relationship Between Oedema, Plasma and Urinary Antidiuretic Hormone in Pre-eclamptic Toxaemia

Clinical Estimate of Oedema	Number of Cases	Presence of Antidiuretic Hormone in Urine	Number of Cases	Presence of Antidiuretic Hormone in the Plasma		
				Positive	Doubtful	Negative
Marked	11	Positive	11	11	0	0
		Negative	0	0	0	0
Moderate	37	Positive	36	36	0	0
		Negative	1	0	1	0
Slight	3	Positive	1	1	0	0
		Negative	2	0	1	1
No oedema	2	Positive	0	0	0	0
		Negative	2	0	1	1

same substance not found in the urine, while a negative urinary finding did not necessarily imply that antidiuretic hormone was not present in the plasma. Figure 11 is of an individual case of pre-eclamptic toxaemia and shows graphically the course of the case from 17 days prior to confinement to one week after. Before delivery antidiuretic hormone could be detected in both the urine and plasma but after delivery the urine became negative and then the plasma failed to show antidiuretic activity. These findings are in keeping with the rapid disappearance of the oedema post-partum.

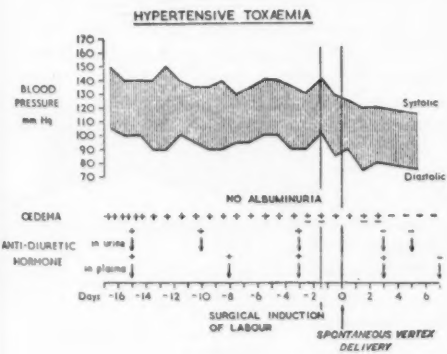

FIG. 11

Pre-eclampsia.

To illustrate the relationship between the antidiuretic hormone and the clinical course of the oedema.

When oedema disappears, post-partum, first the urine and then the plasma become negative.

When we now look at the results in the group of eclamptic patients these are as would be expected from the results obtained in the pre-eclamptics. Fortunately or unfortunately none of the pre-eclamptic patients who were under investigation went on to the convulsive stage. The results reported here are all of patients who were admitted to hospital after at least one convulsion. It is impossible therefore to state whether antidiuretic hormone was present in the blood or urine before the convulsion. However the urine present in the bladder on admission was examined and the opportunity was taken to obtain a sample of blood as soon as was practicable. Figure 12 illustrates the findings in a typical case of eclampsia. This patient was admitted following one fit and had a second shortly after admission. She was in labour on admission and was treated with Bromethol. Some eleven hours after the first fit the patient was delivered by low forceps of a child which was alive and well. It will be noted from the antidiuretic results in the urine and in the plasma that this substance persisted for some considerable time after delivery and that first the urine became negative and then the plasma findings also became negative. Again the alteration in

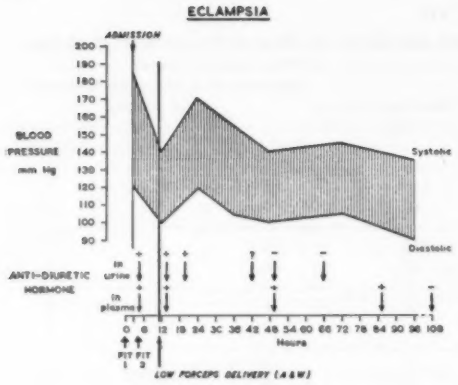

FIG. 12

Eclampsia.

To illustrate the rapid disappearance of the antidiuretic hormone, first from the urine, then from the plasma, in association with clinical development.

the antidiuretic assay from positive to negative coincided with the disappearance of the oedema. Table VIII contains details of the 6 cases of eclampsia examined and shows the time of disappearance of antidiuretic hormone from the urine and the plasma. These times are taken as accurately as possible from the onset of the first seizure. In the first five cases reported above the time of disappearance of antidiuretic hormone from the urine and the plasma is fairly constant but in the sixth case antidiuretic hormone persisted in the urine for a minimum of 152 hours and in the plasma for a minimum of 246 hours.

Figure 13 is a diagrammatic representation of this patient's course whilst in hospital. Once again one fit occurred before admission and the second shortly thereafter. The patient was treated with Bromethol, seemed to respond satisfactorily and after some time sedation was lightened. Approximately 120 hours after the first fit a further series of five seizures occurred. Thereafter the patient's course was uncomplicated. If you now look at the status of this patient as regards antidiuretic hormone it will be noted that this substance persisted in the urine some 150 hours after the first seizure and in the plasma for some 250 hours. These times are in fact approximately three times as long as has been found in the other cases but prior to the second convulsive episode the urinary persistence was already twice as long and one wonders whether, if the significance of this finding had been appreciated at the time, the further series of convulsions could have been avoided.

The results as reported up till the present have established the presence of antidiuretic hormone of the posterior pituitary gland in the blood and urine of toxaemic pregnant women and as this substance could not be demonstrated

TABLE VIII

Time of Disappearance of Antidiuretic Hormone from Urine and Plasma in Eclampsia

No. of Fits	Time of Disappearance of Antidiuretic Hormone (from first fit)	
	Plasma	Urine
1	75 to 82 hours	51 to 62 hours
3	78 to 101 hours	44 to 54 hours
2	97 to 115 hours	57 to 69 hours
2	85 to 108 hours	42 to 50 hours
1	92 to 114 hours	48 to 56 hours
7	246 to 262 hours	152 to 195 hours

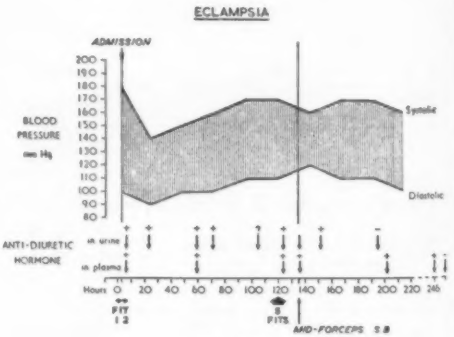

FIG. 13

Eclampsia.

To illustrate the persistence of antidiuretic hormone in the plasma and urine.

Fits recurred and thereafter disappearance of the antidiuretic hormone and clinical improvement occurred.

in the blood or urine of the majority of cases of normal pregnancy, it would appear that a significant difference has been shown. I now tried to see whether I could show the existence of any physiological mechanism which could possibly account for these findings. As I have previously said it is known that the output of antidiuretic hormone from the posterior pituitary gland is under several controls. The most important of these is the osmotic pressure of the blood acting upon osmoreceptors in the hypothalamus (Verney, 1947). Further it is known that certain of the solutes which contribute to the osmotic pressure of the blood are more evocative of antidiuretic response than are others, this latter fact being due to the relative permeability or otherwise of the osmoreceptors to different solutes. (For example, when freely permeable to glucose it does not result in antidiuretic hormone output; when impermeable to sodium chloride there is an antidiuretic hormone output.)

In an attempt to determine whether this mechanism operated in pre-eclamptic toxaemia the following experiment was carried out. Arterial blood was withdrawn by femoral artery puncture. This arterial puncture was conducted under similar conditions and at approximately the same time, to exclude as many variables as possible. Arterial blood was employed for several reasons amongst which was the known, rapid inactivation or utilization of the antidiuretic hormone *in vivo* and the femoral artery was selected in an effort to obtain a sample of blood as similar as possible to that present in the renal arteries and therefore that acting upon the kidneys. Approximately 20 ml. of blood were withdrawn and this blood separated into two portions. The first portion was transferred to a heparin tube and the plasma immediately separated and submitted to assay of antidiuretic content. The rat was prepared and known to be reactive prior to femoral puncture. The second portion of arterial blood was allowed to clot, the serum separated and the osmotic pressure, electrical conductivity, sodium, potassium, and chloride concentrations determined. The osmotic pressure was assessed by the depression of the freezing point of the serum as compared with distilled water and was carried out in duplicate. Table IX shows the results of these estimations in two groups of patients, the one toxaemic and the other normal. From the table it will be seen that the mean depression of the freezing point in the two groups is very similar and on statistical analysis this slight difference did not prove to be significant. The electrical conductivity of the serum was assessed as a measure of the total ionic concentration of the serum and hence an indirect measure of the osmotic pressure. Once again little difference was found between the two groups and this difference was again not significant. No statistical difference was found between the mean concentration of sodium in the two groups nor in the mean concentration of potassium but a statistical difference was found in the mean concentration of chloride present and of course an obvious difference was found between the antidiuretic titre of the two groups of patients. When the difference in the mean concentration of chloride between the two groups is translated into its effect upon

TABLE IX

Biochemical, Biophysical and Antidiuretic Hormone Estimations on Two Groups of Patients, the One Normal, the Other Pre-eclamptic

Group	Mean Depression of Freezing Point °C.	Mean Electrical Conductivity R.Ohms	Mean Concentration of Sodium Meq/litre	Mean Concentration of Potassium Meq/litre	Mean Concentration of Chloride Meq/litre	Antidiuretic Titre Milliunits/ml.
Toxaemic	0·561	0·156	133	4·33	106	0·025 to 0·160
Normal	0·553	0·155	135	4·37	102	Nil

osmotic pressure it is found that the effect is of greater magnitude than that which Verney (1947) found to be experimentally effective in producing an antidiuretic response in animals. However, when an attempt was made to relate graphically the chloride concentration in any given case with the antidiuretic titre, no direct correlation was discernible and the interpretation of this increased chloride concentration must be considered doubtful and no definite conclusion can be drawn as to causation of the excess antidiuretic hormone.

That lesions similar to these seen in eclampsia can be produced in suitably prepared animals by the use of antidiuretic hormone has been shown by Govan (1952) and these could be reproduced in the present experiments.

In the remaining few minutes I would like to discuss the significance of these findings. The evidence presented establishes, I believe, that this substance is in fact the antidiuretic hormone of the posterior pituitary gland and therefore I do not intend to spend any further time on this point.

That the substance is but rarely found in the urine or plasma of the normal pregnant patient and almost consistently present in the urine and plasma of the pre-eclamptic shows that an excess of antidiuretic hormone exists in this latter condition. Obviously an excess of antidiuretic hormone may be due either to an increased production or a decreased destruction. Taking the question of increased production first. Is there any evidence in support of this? The stimuli known to produce an increased output of antidiuretic hormone have been mentioned previously. Of these stimuli suckling, fainting, shock, haemorrhage, anaesthetic agents and drugs, including nicotine, can be immediately discounted as these stimuli are not operative in the cases under consideration. Emotional stress equally does not seem a very probable cause of the consistent finding of antidiuretic hormone in the plasma and urine. This leaves variation of the osmotic pressure as the remaining stimulus and as I have already shown there is no significant variation in the total osmotic pressure and such variation as exists in the osmotic pressures of the various solutes is due to chloride. While this variation is of such a nature as to be capable of producing a response of increased antidiuretic hormone excretion it proved impossible in the individual case to relate the chloride concentration to the antidiuretic titre in the plasma. The absence of any such correlation would seem to necessitate an alteration in the sensitivity of the hypothalamic osmoreceptors were this to be the explanation of the increased antidiuretic hormone output. That this alteration may be possible is shown by the work of Baldes and Smirk (1934). Before however accepting such a hypothesis is there any alternative explanation which may be advanced for the apparent increase in antidiuretic hormone in pregnancy toxaemia. The destruction of the hormone is partly by urinary excretion and partly by metabolism in the liver. That a failure of urinary excretion is not the solution is apparent in the light of the finding that antidiuretic hormone can be detected in the urine from cases of acute toxaemia of pregnancy but is not detectable in an equal volume of urine from normal gravida. While it might be held that the increased antidiuretic hormone level is due to the kidney's inability to clear the blood of antidiuretic hormone the quantitative estimates did not support this theory. The possibility of a failure of liver metabolism of the antidiuretic hormone must also be borne in mind. Particularly so when it is accepted that pre-eclamptic toxaemia alters hepatic function. None of these explanations however would seem in any way to explain the excess of antidiuretic hormone circulating in the blood of a case of pre-menstrual tension. A further method of destruction of antidiuretic hormone has been suggested by McCartney *et al.* (1952) and more recently by Hawker (1957). These workers have shown that the blood of the normal pregnant patient contains a substance capable of inactivating the antidiuretic hormone of the posterior pituitary gland. Hawker was unable to demonstrate this inactivating substance either in the blood of the toxaemic pregnant patient or in the blood of the non-pregnant female and has suggested that this substance may be in the nature of an enzyme.

The evidence tends to suggest therefore that the excess antidiuretic hormone present in the pre-eclamptic patient may not in fact represent

an excess production of the hormone but rather that a destructive enzyme apparently peculiar to the gravid state is absent in cases of toxaemia of pregnancy and hence a build up of antidiuretic hormone occurs in the blood. This would also account for the almost constant urinary excretion in pre-eclamptic toxaemia. This possibility is at present under investigation.

Whatever the cause of this increased antidiuretic hormone in toxaemia of pregnancy it would obviously explain some of the renal changes. The impaired elimination of water can be explained as a function of excess antidiuretic hormone and the impaired elimination of urea, sometimes found, can be explained by the slower tubular flow of glomerular filtrate and hence the increased back-diffusion of urea; this back-diffusion of urea being inversely proportional to the tubular flow.

One must also consider the action of the antidiuretic hormone in relation to other hormonal factors.

That the pregnant woman and, in particular, the pregnant woman with toxaemia, shows an increased susceptibility to posterior pituitary extract has been previously mentioned. Govan and Mukherjee (1950) showed that this sensitivity was due to anterior pituitary gonadotrophins and this might suggest hyperactivity of the entire pituitary complex rather than of any particular portion. It has also been possible to produce lesions closely resembling those found in human eclampsia in the liver and kidneys of animals sensitized with anterior pituitary gonadotrophins and treated with posterior pituitary extract. These animals become oliguric and convulsive before death. These facts seem to lend point to the statement of Harris (1948) that there is normally a balance between the specific antidiuretic action of the neurohypophysis and the diuretic influence of the adenohypophysis and suggests that the fluid retention in pre-eclampsia may rest in an upset of this balance.

It is obvious from the work done in recent years that the adrenals play some part in pre-eclamptic toxaemia. The action of antidiuretic hormone is considerably modified in such conditions as Addison's disease and Slessor (1952) suggests that the slow response of these patients to water ingestion is in fact due to circulating antidiuretic hormone and only when this hormone is destroyed naturally by time or by the administration of cortisone does diuresis occur. From this he concludes that cortisone mediates the destruction of posterior pituitary antidiuretic hormone. This conclusion has been supported by the work of Birnie *et al.* (1949) while Lockett (1952) has shown that adrenalectomized animals show an increased sensitivity to pituitary extract. There is no evidence, however, to support a reduction of cortisone output in pre-eclampsia and certainly the administration of cortisone has proved anything but beneficial in these cases.

Another mechanism was suggested by Lloyd and Lobotsky (1950). They found that the antidiuretic activity of the serum and the urinary corticosteroid level both bear a relationship to the state of water balance. The comparative proportions of these substances are of greater significance than the absolute values of either one of them. Regardless of the absolute values if the antidiuretic hormone is relatively greater than the corticosteroid then water retention occurs. They also found the converse to apply in diuresis. In these findings may lie the explanation of the failure to correlate the severity of the toxaemia of pregnancy with the level of the antidiuretic hormone in the plasma. A parallel estimation of the corticosteroids present might have allowed a ratio to be developed.

More recently Lloyd (1958) and Pickford (1958) have published results which show that oxytocin may in fact be a cause of vasospasm in the presence of oestrogens and Byrom and Pratt (1959) have succeeded in producing renal cortical necrosis in animals treated with oestrogens and oxytocin. These latter workers add however that the dose of oxytocin required far exceeds what may reasonably be expected of natural secretion.

In view of the known joint liberation of antidiuretic and oxytocic hormones in response to the same stimulus, the possibility that these two hormones may act synergistically in toxaemia of pregnancy must be considered.

Whatever the truth of these various suggestions may be I submit that two facts have been clearly demonstrated. The first that in pre-

eclampsia and eclampsia there exists in the blood and urine an antidiuretic substance which is not to be found in the blood or urine of the vast majority of cases of normal pregnancy. Secondly, that this antidiuretic substance is in fact the antidiuretic hormone of the posterior pituitary gland. Whatever the action of this antidiuretic hormone is in pre-eclampsia, and only a few of the possible theories have been touched upon today, I feel that in a disease whose clinical diagnosis rests upon albuminuria, hypertension and oedema and with characteristic tissue lesions it is impossible to exclude from consideration a substance capable of producing hypertension and water retention as well as similar lesions in the liver and kidneys of experimental animals. Particularly is this so when an excess of this very substance can be shown to exist in these cases.

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THE ONSET OF STRESS INCONTINENCE

BY

WINIFRED J. A. FRANCIS, M.D., M.R.C.O.G.

From the Department of Obstetrics and Gynaecology, The University of Liverpool

ALTHOUGH, like genital prolapse, stress incontinence is sometimes seen in nulliparous women, the disability is generally regarded as being mainly the result of an obstetrical injury to the tissues around the urethra and urethro-vesical junction. It is commonly noted in women reporting for postnatal examination, and those who complain of it later in life attribute its origin to one or other pregnancy. They and their medical attendant then tend to assume that it dated from the confinement rather than the pregnancy itself. During the course of an investigation into the voiding habits of pregnant women, reported elsewhere (Francis, 1960), it became clear that, contrary to the general impression, the symptom was often present during pregnancy, even a first pregnancy. This observation led to more detailed enquiry into the time of onset of the stress incontinence.

MATERIAL AND METHODS

Four hundred unselected patients attending a hospital antenatal clinic were specifically studied during pregnancy and after. All of these women were questioned carefully as to their voiding habits, in particular in regard to stress incontinence. The group comprised 222 primigravidae and 178 multigravidae. All of the women who admitted to stress incontinence, a total of 268, were subjected to cystometry to confirm the presence and to assess the severity of the symptom.

In addition to the total 400 women questioned, urethrocystography was carried out on a further 83 women. These comprised two groups:

(1) Thirty-three pregnant women with stress incontinence.

(2) Fifty pregnant women with good bladder control.

All of these patients had, for some obstetric reason, to have a lateral pelvic radiograph in late pregnancy and the opportunity was taken to introduce radio-opaque medium into the bladder prior to radiography. The exposure was made with the woman standing and straining to raise the intra-abdominal pressure. All these 83 patients consented to one further urethrocystograph being taken two days after their delivery. The radiation hazard, although explained to the patient, was calculated to be minimal. Only a small area at the urethro-vesical junction was irradiated and that at a time when the ovaries are high in the abdomen beside the recently delivered uterus.

In the puerperium a single radiograph was taken with the woman raising the intra-abdominal pressure while sitting on the special chair described by Roberts (1951, 1952). Two of the thirty-three women who suffered stress incontinence were also subjected to urethrocystography one year after delivery because at that time they were complaining so bitterly that surgical treatment became necessary.

The technique used for lateral urethrocystography was that described by Roberts (1951, 1952, 1953) and Jeffcoate and Roberts (1952b, 1954, 1956). An upright Bucky diaphragm was employed and the exposure was 120 kilovolts at 200 milliamperes for 0·5 seconds, at a tube film distance of not more than 36 inches. A 4 mm. aluminium filter and extending cone were used to reduce scatter. One hundred and twenty millilitres of 12·5 per cent sodium iodide and 15 ml. of fluid "neohydriol" was the usual amount of radio-opaque

medium employed. Special care was taken to warm the medium and run it in slowly to avoid irritating the bladder and causing detrusor contraction. The amount of medium had to be reduced to 80 to 100 millilitres in some women in late pregnancy, as larger amounts of fluid produced detrusor activity as shown by a desire to void and by the radiographs (Fig. 1). A few women also could not tolerate sodium iodide. In these cases ½ strength barium sulphate (Micropaque, Damancy and Co.) was employed.

The radiographs obtained with so weak a solution were not entirely satisfactory but a stronger solution, by virtue of its weight, causes irritation of the bladder as pointed out by Jeffcoate and Roberts (1956).

The Incidence of Stress Incontinence

One hundred and eighteen primigravidae (53 per cent) and 150 multigravidae (85 per cent) experienced stress incontinence of some degree during pregnancy (Table I).

TABLE I

Incidence of Stress Incontinence During Pregnancy

	Number	Stress Incontinence	
		Present	Not Present
Primigravidae	222	118 (53%)	104
Multigravidae	178	150 (85%)	28
Total ..	400	268 (67%)	132

On further questioning, however, it became clear that 49 primigravidae (42 per cent) had throughout life suffered occasional loss of urinary control. This is in agreement with the findings of Nemir and Middleton (1954) who reported that, out of 1,327 young unmarried nulliparous women, 45 per cent had slight and intermittent, and a further 5 per cent had troublesome, stress incontinence. Duncan's (1956) figures were higher. He found that 87 out of 134 young nulliparae (65 per cent) suffered stress incontinence; in 70 (52 per cent) it was of occasional occurrence, but in 17 (13 per cent) it was frequently experienced.

Time of Onset

Stress incontinence rarely, if ever, appears for the first time *after* childbirth. It commences, if only in slight degree, either before or during the pregnancy. Of the 150 multigravidae with stress incontinence 60 (40 per cent) noted it for the first time in the pregnancy under observation. Seventy (47 per cent) had had incontinence in a previous pregnancy with relief after delivery, while 19 (13 per cent) had had stress incontinence during and apart from previous pregnancies. None of the multiparous patients suffered stress incontinence *for the first time* during a previous puerperium. It had always commenced while they were nulliparous or during one of their pregnancies, not necessarily the first. Once present it reappeared in a gradually worsening degree with each subsequent pregnancy. Between pregnancies it amounted at first to no more than an occasional loss of control in the face of severe stress. Ultimately, however, in a few women it gradually became more troublesome until it was a persistent problem even in the non-pregnant state. These findings are not in agreement with Ullery (1953) and other authors who regard stress incontinence as a common sequel to labour, showing itself either in the puerperium or after the menopause when the supports are further weakened by atrophy. The women in this series who had stress incontinence in the puerperium all suffered the symptom during pregnancy. Its onset was distributed equally between all the trimesters (Table II).

TABLE II

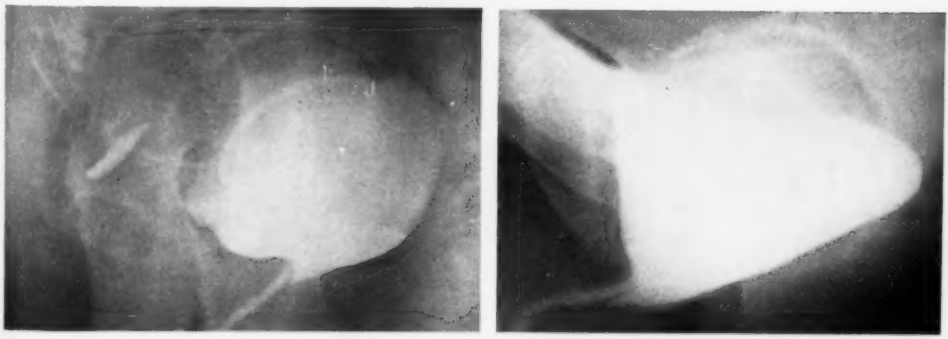
Time of Onset of Stress Incontinence

First Trimester	Second Trimester	Third Trimester
66 (30%)	68 (31%)	85 (39%)

Of the 219 patients in whom stress incontinence commenced or recommenced during the pregnancy under observation 66 (30 per cent) noted its onset in the first trimester, 68 (31 per cent) in the second and 85 (39 per cent) in the third trimester. Once present, the severity of the

FIG. 1

Lateral urethrocystograph in a gravida-2, 39-weeks pregnant. The radiograph was exposed with the patient "resting easily" but the appearances are those of early micturition. Detrusor contraction is occurring as evidenced by the shape of the bladder and the crenations in its walls and this has resulted in opening of the upper urethra with obliteration of the posterior urethro-vesical angle. The total amount of sodium iodide (12·5 per cent) and "neohydriol" used was 100 millilitres. This proved too large a quantity for this particular patient and caused bladder irritation. Smaller amounts of media did not produce this picture.



(*a*) (*b*)

FIG. 2

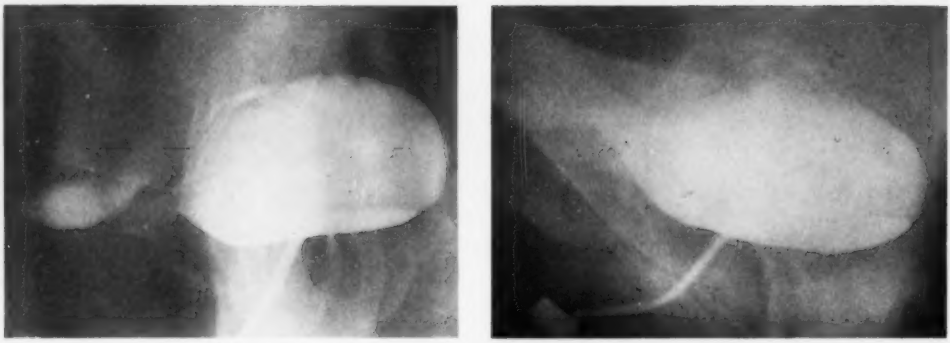
Lateral urethrocystography in a gravida-6, (*a*) at term and (*b*) one year after delivery. This patient suffered severe stress incontinence both during pregnancy and after.

(*a*) The catheter is outlining the urethra. The patient is standing and straining to raise the intra-abdominal pressure. Some of the medium has leaked into the upper urethra. There is loss of the posterior urethro-vesical angle.

(*b*) The patient is sitting and straining to raise the intra-abdominal pressure. The urethra is marked by a catheter. Fluid is entering the upper urethra and there is loss of the posterior urethro-vesical angle. The woman had performed pelvic floor exercises, using Kegel's perineometer, for one year with no relief of the stress incontinence.

FIG. 3

Lateral urethrocystograph in a primigravida at term. The patient is standing and straining to raise the intra-abdominal pressure. There is loss of the posterior urethro-vesical angle. This woman suffered stress incontinence during pregnancy, but obtained relief immediately after delivery.



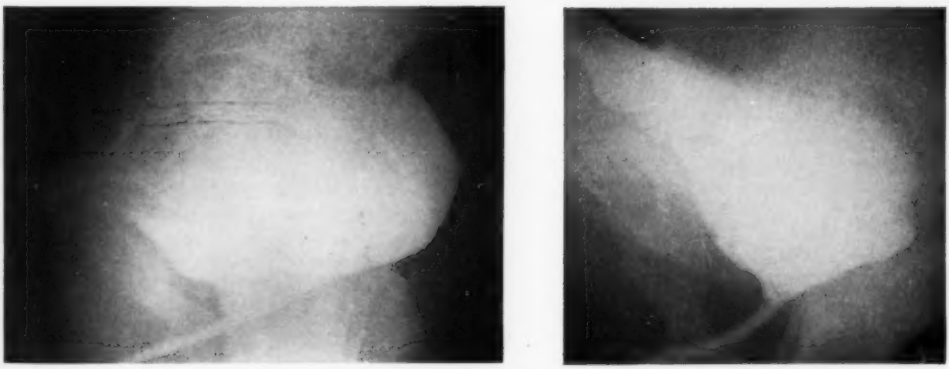
(*a*) (*b*)

FIG. 4

Lateral urethrocystography in a primigravida, (*a*) at term, (*b*) 48 hours after delivery. This patient had good bladder control.

(*a*) The patient is standing and straining to raise the intra-abdominal pressure. The urethra is outlined by a catheter. The bladder has assumed the hour-glass shape frequently seen in late pregnancy. There is a good posterior urethro-vesical angle.

(*b*) The patient is sitting and straining. The urethra is outlined by a catheter. Little change is noted from the previous radiograph. The posterior urethro-vesical angle is maintained.



(*a*) (*b*)

FIG. 5

Lateral urethrocystography in a gravida-1, (*a*) at term, (*b*) 48 hours after delivery. This patient suffered stress incontinence during pregnancy which persisted in mild degree in the puerperium.

(*a*) The woman is standing and straining to raise the intra-abdominal pressure. The urethra is outlined by a catheter. There is loss of the posterior urethro-vesical angle.

(*b*) The woman is sitting and straining. The urethra is outlined by a catheter. The appearance of the urethro-vesical junction is unchanged from that in late pregnancy. There is "absent posterior urethro-vesical angle".

symptom generally increased progressively until term.

The Persistence of Stress Incontinence After Delivery

All the 400 patients were followed through labour and the puerperium, and those with stress incontinence for as long as 6 months. No woman developed loss of bladder control for the first time after delivery. Of those women who had stress incontinence during pregnancy, 244 (91 per cent) reported almost complete relief immediately, or within a few days, after delivery. Thereafter they had no incontinence except when they developed a cough. This occasional incontinence occurred in 93 (38 per cent) women. The remaining 24 (9 per cent) continued to suffer urethral incompetence, of severe degree in 15, as a permanent disability. Twenty of the patients who suffered stress incontinence during pregnancy were delivered by Caesarean section. Of these none continued to have stress incontinence in the puerperium.

There were 40 women who, having suffered stress incontinence during the observed pregnancy and being relieved afterwards, conceived again during the follow-up period. All noted a return of stress incontinence of increased severity in the next pregnancy.

The Value of Pelvic Floor Exercises

Kegel (1948a, 1948b, 1949) and Jones (1951) cured many patients with stress incontinence, even of severe degree, by teaching them to contract the pubo-coccygeus muscles against the resistance of a soft rubber tube connected to a manometer. Kegel's perineometer was used in the 24 patients who continued to suffer stress incontinence after delivery. The exercises were started as soon as the woman noted the persistence of stress incontinence in the puerperium. This was usually apparent for certainty about the fifth day following delivery. Most of the patients were able to use the perineometer satisfactorily when they were discharged home on the tenth day post-partum. They continued to exercise at home and were seen at regular intervals until six months after delivery.

The exercises were not found to be of great value. None of the patients with severe stress incontinence obtained any alleviation of the symptom, nor in the 2 cases studied before and after exercises were the radiographic appearances of the urethro-vesical junction altered by the physiotherapy (Figs. 2a and 2b). A few women with mild stress incontinence noted an improvement, but the incontinence returned if they developed a cough.

The Anatomical Changes Associated with Stress Incontinence During Pregnancy and the Puerperium

Among the 83 women, who had lateral urethrocystography combined with essential obstetric radiography in late pregnancy, 33 suffered stress incontinence and 50 women had good bladder control. The findings confirmed those described by Roberts (1951, 1953), Jeffcoate and Roberts (1952a, 1952b, 1954, 1956), Bailey (1954, 1956), Janssens (1956, 1958) and Jeffcoate (1957, 1958) for stress incontinence in the non-pregnant woman. The radiological sign of "absent posterior urethro-vesical angle" was a striking feature in patients with stress incontinence. Thirty out of the 33 women (90 per cent) who suffered stress incontinence showed loss of the posterior angle (Fig. 3), a figure similar to that reported by Jeffcoate and Roberts (1952b, 1956) and Jeffcoate (1957, 1958). The angle was absent in 4 out of the 50 women (8 per cent) with good control.

The radiographs exposed on the second day of the puerperium invariably showed a urethro-vesical junction similar to that in late pregnancy (Figs. 4 and 5). Indeed the anatomy of the urethra and bladder returns to its preparturitional state almost immediately after labour. This is in accord with the finding of Braune (1872) and Barbour (1889) who studied frozen sections, and of Malpas *et al.* (1949) and Kantor *et al.* (1949) who carried out urethrocystography before, during and after labour. Thirty-four of the 83 patients studied by radiography showed no posterior urethro-vesical angle during pregnancy, and all of them failed to show it in the early puerperium. Four of

these suffered troublesome stress incontinence in the puerperium and afterwards but the other 30 managed to control the bladder reasonably well unless they developed a cough; the weakness was then invariably revealed. This is possibly explained by the dual sphincter control postulated by Roberts (1951, 1953), Jeffcoate and Roberts (1952a, 1952b, 1956) and Jeffcoate (1957, 1958). The woman contracts her compressor urethrae if she has sufficient warning and so avoids the occurrence of stress incontinence. It seems likely, however, that the majority of women do show recovery of the urethro-vesical angle at some time later in the puerperium, otherwise the radiographic appearances said to be typical of stress incontinence would be found in some 60 per cent of all non-pregnant women. The time at which the angle reappears, if it does reappear, was not investigated, since it would have necessitated repeated radiation exposures during several months. In the two patients with persisting severe stress incontinence who had urethrocystograms performed one year after delivery, the posterior urethro-vesical angle did not return despite the regular use of Kegel's perineometer.

Discussion and Conclusions

The findings in regard to the onset of stress incontinence of urine give rise to conclusions which are contrary to general opinion. This may be because they represent a current and prospective study rather than a retrospective one.

The investigation confirms those of others who found that approximately 40–50 per cent nulliparous women experience stress incontinence, generally of slight degree. These women, when they conceive, invariably experience an exacerbation of the symptom during pregnancy. There are other women who first experience stress incontinence during pregnancy but in few if any can the onset of the symptom be attributed to childbirth itself, that is it does not begin in the puerperium. The stress incontinence of pregnancy is characterized by the same radiographic appearance of the urethro-vesical junction as is the stress incontinence of the non-pregnant woman. The question arises as to why pregnancy causes this symptom or makes it worse. It may be that it is related to the atony of all the involuntary musculature in the pelvis and elsewhere but this is conjecture and so far without proof.

The woman with stress incontinence during pregnancy may obtain relief within a short time of delivery and this happens in 91 per cent cases. The relief is not attended by an immediate return to normal of the anatomy of the urethra and bladder base; whether this occurs later is unknown. In many cases, when another pregnancy supervenes the symptom returns—usually in more troublesome form. Each successive pregnancy (not labour) tends to cause further deterioration in bladder control so that ultimately the woman is left with permanent incontinence, at first slight and then severe. This, again, may be made worse by advancing age and probably senile atrophy. Women in whom the symptom persists in severe degree after pregnancy continue to show the typical radiographic changes in the anatomy of the urethro-vesical junction. The general conclusion therefore is that those women who complain of stress incontinence in middle life are destined to do so from an early age. Pregnancy rather than labour reveals an intrinsic defect in the sphincter mechanism.

Summary

Four hundred unselected women (222 primigravidae and 178 multigravidae) attending a hospital antenatal clinic were questioned during and after pregnancy regarding stress incontinence.

Cystometry was performed on all the 268 patients who complained of this symptom.

Urethrocystography was carried out on a further 83 pregnant women, 33 of whom suffered stress incontinence and 50 with good bladder control.

The findings were:

(1) Approximately 40 per cent of primigravidae give a history of having had occasional stress incontinence before pregnancy.

(2) Stress incontinence of urine rarely, if ever, appears for the first time after childbirth.

It commences, if only in slight degree, either before or during pregnancy.

(3) The woman who has had stress incontinence before pregnancy is invariably worse during pregnancy.

(4) Incontinence present during pregnancy tends to disappear in the puerperium. It recurs, however, with each pregnancy and becomes progressively worse. Ultimately, and in certain women, it remains after delivery to become a persistent complaint.

(5) The radiographic sign of "absent posterior urethro-vesical angle" characterizes 90 per cent of cases of stress incontinence seen during pregnancy, as it does in the non-pregnant state. The angle does not reappear immediately after delivery even though the patient recovers reasonably good bladder control. The time at which it does reappear (assuming that it does) was not studied because of the radiation hazards involved.

(6) It would seem that those women who develop stress incontinence in middle life are destined to do so from an early age but that pregnancy, rather than parturition, reveals the defect and makes it worse.

Acknowledgments

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PLACENTA EXTRACHORIALIS (PLACENTA MARGINATA AND PLACENTA CIRCUMVALLATA)

A Factor in Ante-partum Haemorrhage*

BY

JAMES S. SCOTT, M.D., F.R.C.S.(Ed.), M.R.C.O.G.

From the Department of Obstetrics and Gynaecology, University of Liverpool and Mill Road Maternity Hospital, Liverpool

PLACENTA extrachorialis may be defined as a condition of the placenta in which the transition from membranous to villous chorion does not occur at the placental edge, the normal site, but at a variable distance within the circumference of the placenta. An alternative way of expressing this is to say that the chorionic plate—that portion of the chorion from which the villi have origin†—is smaller in area than the basal (or decidual) plate of the placenta. There is thus placental tissue present beyond the limits of the chorionic plate—*placenta extrachorialis*.

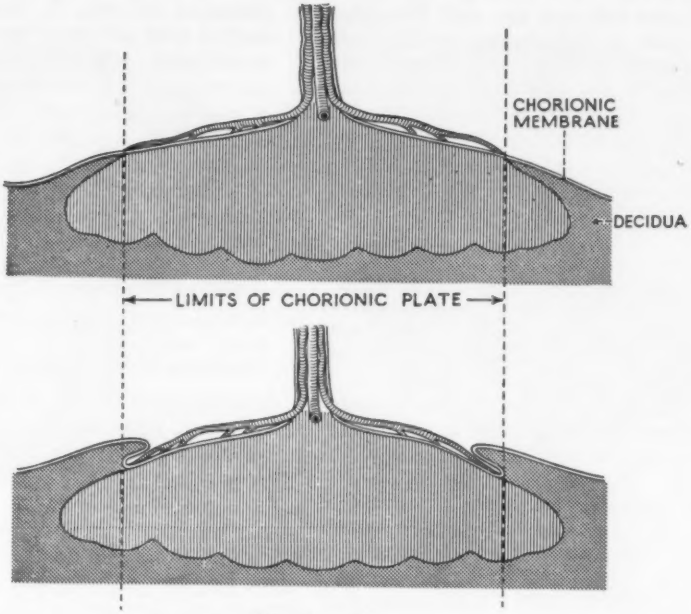
At the margin of the chorionic plate there may only be a thin fibrinous ring where the foetal vessels appear to terminate (placenta marginata, Fig. 1) or there may be a fold towards the centre of the placenta (placenta circumvallata, Fig. 2). The fold may be present only in part of the circumference (Torpin, 1953; Pinkerton, 1956). Such a placenta is then both "marginate" and "circumvallate" (Fig. 3). It is, therefore, not possible to distinguish between these two types of placentae and it was because of this that Robert Meyer in 1912 grouped both anomalies under "placenta extrachorialis". This term is used in this paper as it is descriptive of the basic anatomical abnormality. Other adjectives which have been used previously for variants within this group include "circum-crescent" (Goodall, 1934), "nappiform" (turnip-like), "encollorata", and "annulus fibrosus".

The modern English literature on the subject of placenta extrachorialis starts with Whitridge Williams's paper on placenta circumvallata in 1927. The condition was, however, recognized long before this. Williams stated that the first description was attributed to William Hunter, though he himself had been unable to trace the original paper.

An Anatomical Description of the Human Gravid Uterus and Its Contents was published in 1794, after Hunter's death. Edited by his nephew Mathew Baillie, it was intended as a companion to his earlier and better known volume of plates on the same subject. On pages 38–39 of the posthumously published description of the plates he writes: "The following peculiarity I have often found in the placenta. Upon its inner surface at more or less distance from the extreme border, there is a projecting brim, of the whitish colour of pleuritic blood, which gives a hollow dish-like appearance to the inside of the placenta. The membranes go off from this brim and the circumference of the placenta is remarkably thick, forming a convex surface (part of the outer surface of the placenta) instead of a thin edge." Though he does not use the term, there is no doubt the condition he is describing is the same as that later labelled "circumvallate". For clarity and simplicity, the description compares more than favourably with any to be found in modern literature.

* A paper based on this study was presented to the Birmingham and Midland Obstetrical Society on 2nd October, 1959.

† Millar (1959) uses the term "chorionic plate" to describe the thin layer of trophoblast which lines the decidua. The same usage appears in American writing and is a possible source of confusion.



FIGS. 1 AND 2

Diagrammatic cross-sections of placentae extrachoriales, Figure 1 without a fold at the edge of the chorionic plate (placenta marginata) and Figure 2 with a fold in this situation(placenta circumvallata). Apart from this the placental anomaly is identical in each type—there is a zone of placental tissue beyond the edge of the chorionic plate.

TABLE I

Recorded Incidence of Clinical Complications with Placenta Circumvallata

	Hobbs and Rollins (1934)	Hobbs and Price (1940)	Hunt *et al.* (1947)	Paalman and Veer (1953)	Morgan (1955)	Pinkerton (1956)
Number of cases	79	150	47	41	204	50
Abortion	43%	22%	17%	—	—	6%
Ante-partum haemorrhage ..	11%	22%	19%	51%	14%	2%
Premature births	—	16%	21%	—	14%	10%
Hydrorrhoea gravidarum ..	—	2·6%	15%	26·8%	—	—
Foetal loss	43%	33%	24%	29%	4%	8%
Post-partum haemorrhage ..	—	—	—	14·6%	22%	22%
Manual removal of placenta ..	—	8%	—		7%	2%

For 150 years following this, until Whitridge Williams's paper in 1927, the condition received little attention from English writers and then Williams came to the conclusion that it had no clinical significance. Since his paper, however, there have been a series of reports relating the anomaly to various clinical conditions the most frequent being ante-partum haemorrhage. The findings in these series are shown in Table I.

Anatomical Features

The following observations are based on a personal study of a large number of placentae extrachoriales, including a consecutive series of 578 which is analyzed statistically later.

The simplest form of this placental anomaly is indicated merely by a thin fibrous ring on the chorionic surface of the placenta (Fig. 4). This is found at a variable distance inside the circumference and marks the edge of the chorionic plate. The chorionic membrane can be separated readily from that portion of the placenta which lies outside the ring (extrachorial placenta). At and within the fibrous circle it is firmly attached and any further attempt at separation will result in tearing. The foetal vessels which ramify over the surface of the chorionic plate are not visible over the extrachorial placental tissue. Placenta extrachorialis may be only partial—the edge of the chorionic plate coinciding with the placental edge for the remainder of the circumference. The only histological characteristic of this simple type is that, beyond the edge of the chorionic plate, the chorion is avascular. These basic features are common to all cases.

Superimposed on this basic pattern, may be several other changes.

(*i*) At the site of the ring there may be an infolding. This may take the form of:

(*a*) A thin translucent fold of membrane which may be deep (Fig. 5). There is little or no blood clot or fibrin deposition and the general placental shape is normal. In these cases, the fold is found histologically to consist primarily of avascular chorionic membrane (Fig. 6). The amnion may or may not take part. Microscopically decidual tissue is usually present and may contribute a complete double layer or merely isolated clusters of cells (Fig. 7). Ghost villi may be evident. In 67 per cent of the folds examined histologically, villi were present but in the vast majority these were degenerate (Fig. 8).

(*b*) A thick membrane fold containing fibrin or blood clot. This creates a raised edge and the classical picture described by William Hunter of a "projecting brim . . . which gives a hollow dish-like appearance to the inside of the placenta" (Fig. 9). Microscopically, blood clot or fibrin in varying proportions is evident, in addition to the other features.

(*c*) A fleshy fold containing chorionic tissue. In these rare specimens, histology shows apparently normal active villi in the fold.

Folds of any of the above types may involve the whole circumference of the chorionic plate or only a part of it.

(*ii*) If there is no fold there may be annular deposition of fibrin or blood clot outside the ring of attachment of the chorionic membrane (Fig. 10). All stages of transition between recent blood clot and old fibrin can be seen in these deposits and there can be little doubt that they all have a haemorrhagic origin. Histological examination shows that the clot or fibrin is deep to the avascular chorionic membrane and has decidual cells on its basal aspect (Fig. 11). Regardless of whether the ring of clot or fibrin lies in a membranous fold or not, it always appears to have originated from the edge of the chorionic plate and not the edge of the placenta.

The basal plate is usually normal in appearance regardless of the extent of deformity of the chorionic surface. On transverse section of the placenta the appearances are not remarkable (Fig. 12). The inter-villous space usually appears normal and, even if there is an extensive peripheral sub-chorial haemorrhage, intrusion upon the functional tissue is slight.

If there is neither fibrinous ring nor membranous fold, the detection of placenta extrachorialis may be difficult. In cases of doubt, the diagnosis is established by separating the amniotic and chorionic membranes and then tracing the chorionic membrane towards the placental edge. In a placenta extrachorialis the membrane will readily strip from the peripheral part of the placenta and tearing only occurs

FIG. 3

Placenta extrachorialis *in situ*. The placenta is attached to the posterior uterine wall. On the right, lower part of the circumference of the chorionic plate a raised fold is evident (placenta circumvallata) while at the left upper margin, there is no fold but there is a rim of placenta beyond the distribution of the chorionic vessels (placenta marginata).

FIG. 4

The simplest form of placenta extrachorialis. The chorionic plate does not extend to the placental margin as can be seen from the absence of foetal vessels.

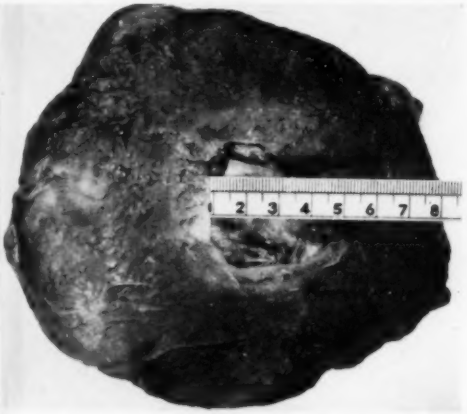


FIG. 5

Placenta extrachorialis showing extreme limitation of the chorionic plate. There is a thin membranous fold at the edge of the plate 1 cm. deep.

FIG. 6

Section of the tip of the simplest type of fold composed of two layers of avascular chorionic membrane. ×62.

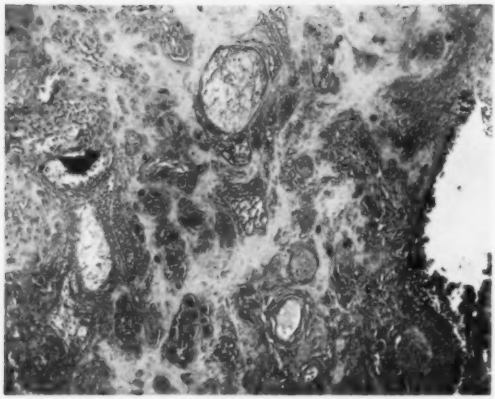


FIG. 7

Section of a membrane fold composed of fibrin, "ghost" villi and many decidual cells. ×62.

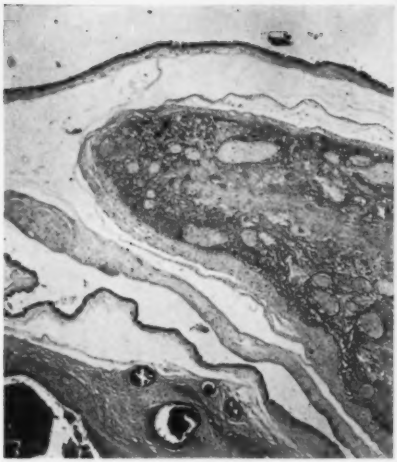


FIG. 8

Section of a fold in which the amnion takes part. The fold contains degenerate villi, decidual cells and fibrin. The vascular chorion of the chorionic plate (bottom) can be clearly distinguished from the avascular chorion forming the fold. ×60.

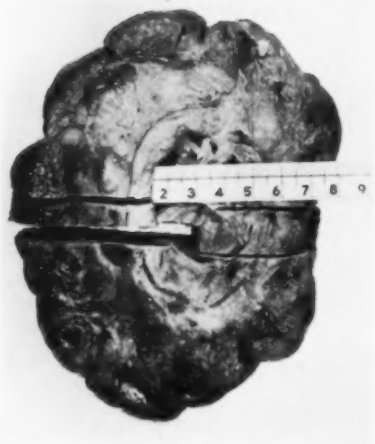


FIG. 9

Placenta extrachorialis with a thick fold at the edge of the chorionic plate containing fibrin.

FIG. 10

Placenta extrachorialis with thick ring of old blood clot at the edge of the chorionic plate. The chorionic membrane has been stripped from the extrachorial placental tissue and it can be seen that further stripping is impossible without tearing the vascular trunks which disappear into the ring of fibrin. The blood apparently originates from the edge of the chorionic plate, not the placental circumference.

J.S.S.

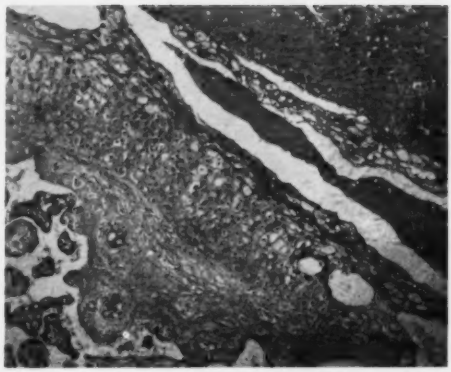


FIG. 11

Section from a placenta extrachorialis with extrachorial haemorrhage. The fibrinous clot is separated from the intervillous space by a layer of decidual tissue. ×57.

FIG. 12

Placenta extrachorialis with a thick collar of clot surrounding a small chorionic plate. Despite the very gross distortion of the chorionic surface, the transverse section has a remarkably normal appearance, showing little or no intrusion upon the intervillous space.

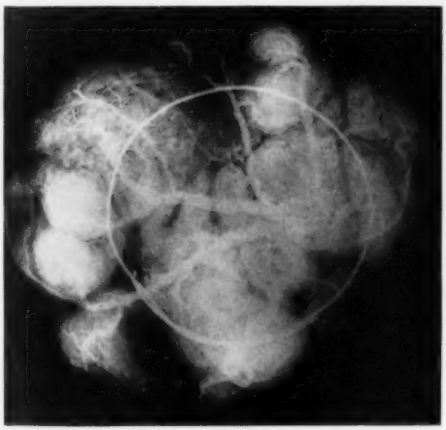


FIG. 13

X-ray of a placenta extrachorialis in which the foetal vessels have been injected with barium sulphate suspension. The shadow of a wire marking the edge of the chorionic plate can be seen. The cotyledons outside this are just as well vascularized as those within.

J.S.S.

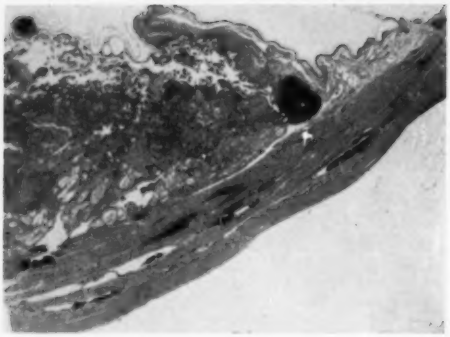


FIG. 14

Section from the margin of placenta extrachorialis *in situ*. At the placental edge a structure can be seen which could possibly be a marginal sinus. ×3·25.

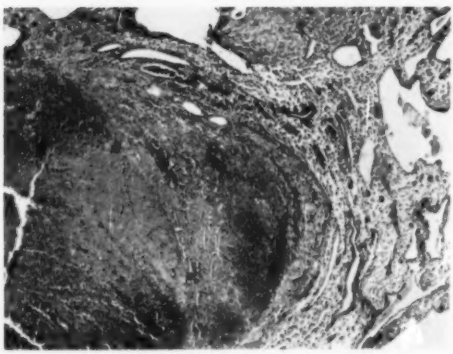


FIG. 15

Microscopic view of the structure seen in Figure 14. It is merely an organizing thrombus. ×28.

when the margin of the chorionic plate is reached (Fig. 10).

The only condition likely to be mistaken for placenta extrachorialis is the entirely unrelated "marginal infarction", in which infarction occurs in the inter-villous space at the circumference of a normal placenta. It is differentiated from placenta extrachorialis by the following features: (1) the inner border of the infarct is irregular—not circular or elliptical as the edge of the chorionic plate always is in placenta extrachorialis; (2) the chorionic membrane cannot be stripped from the surface of the infarcted area; (3) foetal vessels can be seen coursing over the infarcted zone; and (4) transverse section shows that the process involves the whole thickness of the placenta.

In view of the widely different reports of previous writers on the clinical effects of placental anomalies of this type, a prospective controlled investigation was carried out.

Investigation

All placentae delivered in Mill Road Maternity Hospital, Liverpool, from 1st October, 1956 to 30th September, 1957, were examined personally without foreknowledge of the happenings in the pregnancy and without the observer having been responsible for the clinical management of the patients concerned. The diagnosis of placenta extrachorialis was made only when a strip of chorionic tissue, at least half an inch in thickness and involving at least a third of the circumference, lay outside the limit of the chorionic plate. Not until the placental findings had been recorded were the antenatal and intranatal records studied. Whenever placenta extrachorialis was found the mother was questioned personally as to her health during the pregnancy. Particular note was made of the occurrence of vaginal haemorrhage at any time during the pregnancy. The previous menstrual history was also obtained. This questioning was carried out between the second and ninth days of the puerperium. In addition 200 women with normal placentae were similarly questioned to serve as controls. The placentae in which the chorionic surface was distorted by annular haemorrhage or fibrin deposits appeared more likely to be associated with clinical effects. Accordingly placentae of this type were classified separately as *placentae extrachoriales with extrachorial haemorrhage*.

Incidence

Out of the 3,161 consecutive placentae examined, 578 (18 per cent) were placentae extrachoriales and of these 271 (47 per cent or 8·6 per cent of the total) showed evidence of extrachorial haemorrhage.

This incidence of placenta extrachorialis is high but it is less than that suggested by Torpin (1953, 1955a) and Pinkerton (1956) writing on placenta circumvallata. (The incidence found by these and other writers is shown in Table II.) Eighteen per cent, however, is a much higher incidence than noted in the routine entries in the patients' case sheets. On checking the mothers' records in this series of 578 placentae extrachoriales, it was found that in only 162

TABLE II

Recorded Incidence of Placental Anomalies of Extrachorial Type

Authors	Bertkau (1912)	Williams (1927)	Hobbs and Price (1940)	Hunt *et al.* (1947)	Paalman and Veer (1953)	Torpin (1953)	Torpin (1955a)	Pinkerton (1956)	Shanklin (1958)	Present Series
Number of abnormal placentae	—	30	150	47	41	—	—	50	36	578
A. Incidence of marginate placentae ..	14%	—	—	—	—	23%	36%	22·5%	—	—
B. Incidence of circumvallate placentae	1·3%	2%	0·7%	0·5%	0·5%	1–1·5%	4%	2·5%	—	—
C. Incidence of extrachorial placentae (A+B)	15·3%	—	—	—	—	24–24·5%	40%	25%	7%	18%

TABLE III

Incidence of Placental Abnormalities
(Percentages in brackets)

Anomaly	Overall Incidence (3,161 placentae)	Incidence in Group Showing Placenta Extrachorialis
Placenta extrachorialis	578 (18·3)	578 (100)
Velamentous cord attachment	47 (1·5)	3 (0·5)
Battledore placenta	62 (2)	8 (1·4)
Succenturiate lobes	55 (1·7)	8 (1·2)
Bipartite placentae	25 (0·8)	Nil
Bilobulate placentae	36 (1·1)	4 (0·7)
Twin placentae	67 (2·1) (49 binovular)	15 (2·6) (all binovular)
Gross chorio-decidual infarction	54 (1·7)	13 (2·2)
Marginal infarction	23 (0·7)	Nil
Amnion nodosum	2 (0·07)	Nil
Old blood clot on membranes	54 (1·7)	45 (7·8)

cases (28 per cent) had the placental anomaly been recorded by the attendant at delivery. The relatively low incidence in hospital statistics is, therefore, explained by failure to examine placentae meticulously as a routine or by failure to record the findings accurately.

ASSOCIATED PLACENTAL ANOMALIES

The occurrence of other placental abnormalities in association with placenta extrachorialis is shown in Table III. In this the incidence of each abnormality amongst all deliveries is shown together with the incidence in the placenta extrachorialis group. The only notable difference is in the frequency of old blood-clot on the membranes. The significance of this is discussed later.

CLINICAL EFFECTS OF PLACENTA EXTRACHORIALIS

An analysis of various clinical features which might be influenced by placenta extrachorialis is given in Table IV. In each case the relation to placenta extrachorialis with extrachorial haemorrhage is also shown separately. The findings of Hobbs and Rollins (1934), Hobbs and Price (1940), Hunt *et al.* (1947), Paalman and Veer (1953), Morgan (1955) and Pinkerton (1956) regarding the incidence of clinical complications with placenta circumvallata, are summarized in Table I.

(a) *Foetal Asphyxia*

The first three features considered in Table IV —foetal death *in utero*, meconium-staining of the amnion and abnormalities of the foetal heart-beat during labour—are all possible

TABLE IV

Analysis of Possible Clinical Effects of Placenta Extrachorialis

	"Normal" Placenta i.e., no Evidence of Placenta Extrachorialis (2,583 cases)	Placenta Extrachorialis (578 cases)	Placenta Extrachorialis with Extrachorial Haemorrhage (271 cases)
Foetal death *in utero*	79 (3·0% of 2,635 babies)*	22 (3·7% of 593 babies)*	14 (5·1% of 275 babies)*
Meconium staining of the amnion	137 (5·3%)	22 (3·8%)	9 (3·3%)
Abnormal foetal heart rate	90 (3·5%)	21 (3·7%)	11 (4·1%)
Average duration of pregnancy	40·2 weeks†	39·5 weeks	39·2 weeks
Average birth weight	7 pounds 5 ounces†	7 pounds	6 pounds 14 ounces
Prematurity by weight (<5 pounds 8 ounces)	250 (9·5% of 2,635 babies)*	63 (10·7% of 593 babies)*	32 (11·6% of 275 babies)*
Post-partum haemorrhage	114 (4·4%)	27 (4·7%)	20 (7·4%)
Manual removal of placenta	23 (0·9%)	4 (0·7%)	2 (0·8%)
Hydramnios	21 (0·8%)	3 (0·5%)	—
Toxaemia of pregnancy	155 (6%)	24 (4·2%)	11 (4·1%)
Threatened abortion	15 (7·5%)†	47 (8·1%)	28 (10·3%)
Ante-partum haemorrhage	77 (3%)	40 (6·9%)	32 (11·8%)

* These figures allow for twin births.

† The figures marked thus were obtained from the series of 200 women with "normal" placentae who were questioned in detail about their pregnancies.

manifestations of foetal asphyxia. It can be seen that there is nothing to suggest that this placental anomaly significantly interferes with the foetal oxygen supply. This may at first seem surprising as the foetal vessels in these placentae do not obviously extend beyond the limits of the chorionic plate, and the latter may be two or more inches within the placental margin. Moreover, there is often considerable fibrin deposition around the edge of the chorionic plate. Radiological studies of placentae extrachoriales, however, in which the foetal vascular tree was injected with radio-opaque medium confirmed the findings of Meyer (1912) that, although vessels are not evident on the surface of the placenta beyond the chorionic plate, the chorionic tissue which lies outside this is just as well vascularized as elsewhere (Fig. 13). Though the foetal vessels pass from view at the edge of the chorionic plate, their course continues uninterrupted at a deeper level in the placental substance. In several of the histological sections foetal vessels could be seen deep in the peripheral placental substance, apparently supplying the extrachorial placental zone. In Figure 10 such foetal vascular trunks can be seen by the naked eye passing from the edge of the chorionic plate into the placental tissue lying outside it.

(b) *Prematurity and Immaturity*

From the data on average duration of pregnancy and on birth weight, it appears that

placenta extrachorialis is not responsible for premature labour or "immaturity", such as occurs with placental insufficiency. The birth weight differences are not statistically significant ($\chi^2=0{\cdot}276$).

(c) *Post-partum Haemorrhage and Retained Placenta*

While there was no increase in the manual removal rate with placenta extrachorialis, post-partum haemorrhage (over 20 ounces) was more common, especially in the placenta extrachorialis with extrachorialic haemorrhage group. In this category there were 20 cases of post-partum haemorrhage (7·4 per cent), compared with 4·4 per cent in the controls. Six (30 per cent) of these haemorrhages, however, were preceded by ante-partum bleeding, compared with 5 per cent in the controls. Correcting for this effect of previous ante-partum haemorrhage, the incidence of post-partum haemorrhage would be 15 or 5·5 per cent. It thus seems that this apparently significant increase in incidence of post-partum haemorrhage is merely due to the frequent occurrence of ante-partum haemorrhage which is discussed later.

(d) *Hydramnios*

Hydramnios did not occur frequently with placenta extrachorialis, compared with the overall figures, the standards adopted for the diagnosis being those of Scott and Wilson (1957). Mention is made of this fact merely because it has been claimed (Plentl and Gray, 1957) that placenta circumvallata is a cause of hydramnios.

(e) *Toxaemia*

Toxaemia of pregnancy was not increased, the standards for this diagnosis being those of Gemmell *et al.* (1954).

(f) "*Hydrorrhoea Gravidarum*"

In two cases women, who eventually delivered placentae extrachoriales with peripheral haemorrhage, drained fluid *per vaginam* for 14 and 8 weeks respectively before delivery. Neither of these patients was investigated in any detail during the antenatal period but they are of some interest in view of the association of so-called "hydrorrhoea gravidarum" with placenta circumvallata recorded by Hobbs and Price (1940), Hunt *et al.* (1947) and Paalman and Veer (1953) (see Table I).

(g) *Abortion*

It is difficult to obtain reliable evidence as to any association of placenta extrachorialis with abortion. Undamaged placentae from abortions are rarely available. During the period of this survey, only 17* abortion placentae of 12–28 weeks maturity were obtained in a condition suitable for study. Four of these showed evidence of placenta extrachorialis (23·5 per cent) though in some it was extremely difficult to decide whether they were examples of placenta extrachorialis. The diagnosis is certainly not possible in first trimester specimens.

McKay and Hertig (1957) state that placenta circumvallata is the one common anatomical anomaly seen in placentae from second trimester abortions. This is in agreement with the present findings on placenta extrachorialis *but* the incidence is not significantly higher than in the mature placentae examined. The placental anomaly cannot therefore be of importance in causing abortion.

(h) *Ante-partum Bleeding*

An increased incidence of ante-partum bleeding in association with placenta extrachorialis was the most striking clinical finding and this is discussed in detail in the following section. It will be seen from Table I that a high incidence of ante-partum haemorrhage was found in all the studies of placenta circumvallata reviewed there, with the single exception of Pinkerton's (1956).

Ante-partum Haemorrhage in Association With Placenta Extrachorialis

(*i*) Signs of Haemorrhage on Placental Examination

As already stated, 271 (46·9 per cent) of the

* These 17 are in addition to the 3,161 consecutive placentae studied. These 17 abortion placentae were obtained from various sources and were in no sense consecutive.

TABLE V

Ante-partum Haemorrhage with Placenta Extrachorialis

	"Normal" Placentae i.e., no Evidence of Placenta Extrachorialis (2,583 cases)	Placenta Extrachorialis (578 cases)	Placenta Extrachorialis with Extrachorial Haemorrhage (271 cases)
Blood clot on the membranes	44 (1·7%)	45 (7·8%)	38 (14%)
Bleeding before 28 weeks	15 (7·5% of 200 women with normal placentae, personally questioned)	47 (8·1%)	28 (10·3%)
Clinical bleeding after 28 weeks ..	77 (3%)	40 (6·9%)	32 (11·8%)*

* This increased incidence of ante-partum haemorrhage in the group of placentae extrachorialis with extrachorial haemorrhage is highly significant statistically ($\chi^2=55{\cdot}1$ (2 degrees of freedom); $P \ll 0{\cdot}001$).

cases of placenta extrachorialis showed evidence of peripheral haemorrhage in the form of extrachorial rings of fibrin or blood clot. Excluding those cases in which there had been clinical ante-partum haemorrhage, old blood clot was present on the membranes beyond the placental margin in 45 specimens (7·8 per cent). Thirty-eight of the 45 were placentae with extrachorial rings of haemorrhage, giving a 14 per cent incidence of blood clot on the membranes in this group. The incidence of blood clot on the membrane in the control placentae examined was only 1·7 per cent (Table V).

(*ii*) CLINICAL ANTE-PARTUM BLEEDING

(a) *Early Pregnancy* (threatened abortion)

Vaginal bleeding occurred before the 28th week in 47 (8·1 per cent) pregnancies from which placentae extrachoriales were obtained. In the placenta extrachorialis with extrachorial haemorrhage group the incidence was 10·3 per cent (Table V). The haemorrhages varied from slight "shows" to a loss of over a pint of blood, which occurred in 2 cases at the 25th and 26th weeks of pregnancy. In the 200 control patients specifically interrogated, haemorrhage prior to the 28th week occurred in 15 (7·5 per cent). This difference is not statistically significant.

(b) *Late Pregnancy*

Vaginal haemorrhage occurred after the 28th week of pregnancy in 40 (6·9 per cent) of the cases of placenta extrachorialis. In the control series the incidence was 3 per cent (Table V). There was a preponderance of late pregnancy haemorrhage in association with placenta extrachorialis with extrachorial haemorrhage—32 cases (11·8 per cent). This is a highly significant increase ($\chi^2=55{\cdot}1$, $P=\ll 0{\cdot}001$). The severity of the haemorrhage was as varied as in early pregnancy.

On analysis the cases could be divided into the following groups:

	Cases
(*i*) Haemorrhage due to placenta praevia (placenta felt at vaginal examination or seen at Caesarean section)	4
(*ii*) Haemorrhage of "abruptio placentae" type (classical signs of concealed haemorrhage)	7
(*iii*) Trivial "shows"	11
(*iv*) Haemorrhage suggestive of placenta praevia but *not* associated with a low-lying placenta	18

The frequency of placenta praevia and abruptio placentae in cases with placenta extrachorialis is so close to the over-all incidence

(see Table VI) as to suggest that the association is merely coincidental. The trivial "shows" reported by 11 women are probably of little importance. Many of these losses would not have come to light had the patient not been questioned directly; some may merely have been normal "shows" due to commencing cervical dilatation. In the controls questioned the incidence of such minor haemorrhages was very similar—7 in 200. One foetal death *in utero* occurred in a case with a trivial ante-partum haemorrhage. It appeared, however, that the death was unrelated to the haemorrhage.

It is the fourth group, cases having had haemorrhage suggesting placenta praevia but not in fact due to this, which is of greatest interest. The 18 cases in association with placenta extrachorialis represent a disproportionately large number as is shown in Table VI. The incidence is more than twice that when the placenta is normal and over 4 times so in the group with rings of extrachorial haemorrhage. It seems, therefore, that placenta extrachorialis and haemorrhage of this type are definitely related and that this relationship accounts for the over-all increase in ante-partum haemorrhage with these placentae.

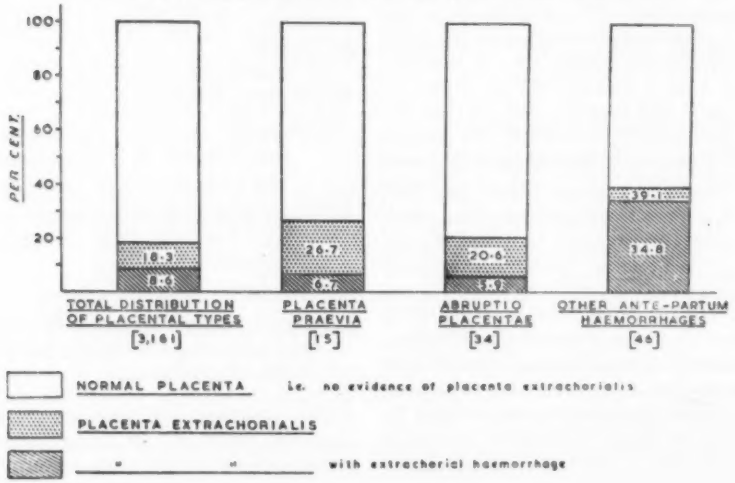
The clinical problems in these 18 cases were considerable. In all, the type of painless ante-partum haemorrhage suggested placenta praevia. In 10 of the 18 the haemorrhage was recurrent. In some, placenta praevia was excluded by the physical and radiological signs but in others this was not possible and the cases had to be managed as ones of placenta praevia. This involved 8 of the 18 patients in varying periods of hospital stay, the longest 11 weeks. Five of the patients had to be examined under anaesthesia to exclude placenta praevia with certainty, while 4 required blood transfusion.

There was one foetal death in this group of 18 cases. A haemorrhage of 6 ounces occurred at the onset of labour, the foetal heart sounds disappeared and a fresh stillborn infant was delivered. There was a complete placenta extrachorialis with a membranous fold involving the whole circumference of the chorionic plate. A considerable amount of fibrin was contained in the fold and this was continuous with organizing blood clot. Approximately 6 ounces of relatively fresh blood clot was also present apparently arising from the edge of the chorionic plate.

In all the placentae in this group it was evident that the haemorrhage had come from

TABLE VI

Placental Type Distribution in Relation to Type of Ante-partum Haemorrhage



the edge of the chorionic plate and *not* the edge of the placenta, which, in these cases, represented the limit of the basal plate (Fig. 10).

Placenta Extrachorialis and the "Marginal Sinus"

Study of placenta extrachorialis leads naturally to consideration of the "marginal sinus" of the placenta. Clinically the type of ante-partum haemorrhage which is related to placenta extrachorialis—painless ante-partum bleeding without the signs of placenta praevia—is identical to that described in the American literature by Sexton *et al.* (1950), Fish *et al.* (1951), Harris (1952), Bartholomew *et al.* (1953), Fish (1955), Ferguson (1955, 1956), Schneider (1958) and Ferguson and Hatton (1959) as being associated with rupture of the marginal sinus.

From a theoretical point of view, the study of placenta extrachorialis offers indirect evidence on the debated questions of the existence and function of the marginal sinus of the placenta. Hamilton and Boyd (1951) say "it seems unlikely that the marginal sinus is a feature of the normal placenta". Other writers, however, particularly from abroad, have not accepted this view. Indeed, Fish (1955) in a monograph mainly concerned with marginal sinus haemorrhage does not mention the controversy over the structure's existence and Ferguson (1955) says there is "no need to defend its existence". These workers apparently accept Spanner's (1935) concept of the maternal blood entering the placenta through central arterioles and then passing outwards towards a marginal sinus from which most of the venous draining occurs. On the other hand, Bøe (1953, 1954) and Ramsey (1956) do take the view that the maternal circulation in the placenta is mainly on a cotyledonary basis and that the marginal sinus is not an important feature.

Fish (1955) defined the position of the marginal sinus as being at the junction of the chorion frondosum and chorion laeve—that is at the site of the marginate or circumvallate ring in placenta extrachorialis. Harris (1952) published illustrations of a placenta circumvallata injected *in situ* and implied that the sinus lay at the level of the circumvallate ring, extending from chorial to decidual surfaces of the placenta. This evidence, however, is not convincing. In cases of placenta extrachorialis, where the edge of the chorionic plate lies far from the circumference of the placenta (see Figs. 4 and 5), it is inconceivable that, if the main channel of venous drainage was so displaced, the placenta would function efficiently. The findings in the present study, however, suggest that the function of such placentae is unimpaired.

In none of the 3,161 placentae examined in this study was any evidence of a marginal sinus found. The same is true of 3 out of 4 intact pregnant uteri made available for study by the courtesy of the Department of Pathology, Liverpool University, with the placenta *in situ*. In the fourth, however, there was a structure which suggested a marginal sinus. This was found in a section from the margin of a placenta extrachorialis *in situ* (Fig. 14). It presents as a discrete area which has the appearance of a circular sinus filled with blood. This lies near the margin of the basal plate, not of the chorionic plate which is approximately $\frac{3}{4}$ inch nearer the centre. On microscopic examination, however, it is seen to be merely an organizing thrombus and not a sinus (Fig. 15). These observations support Hamilton and Boyd's contention that a marginal sinus does not exist as such and are in keeping with Bøe's (1953, 1954) idea that the maternal circulation is mainly cotyledonary.

To deny the existence of the marginal sinus is not to say that the syndrome of "marginal haemorrhage" does not occur clinically. In fact, haemorrhage of this type constituted 46 out of a total of 95 cases of ante-partum haemorrhage occurring in the hospital during the period under review. In 18 of the 46 cases the placenta was extrachorial in type and it seems that the anomaly favours the occurrence of this type of bleeding (Table VI).

It would be unfortunate if a clinical entity fell into disrepute through being mis-labelled in terms of a non-existent anatomical structure. All haemorrhages of this type, whether in association with placenta extrachorialis or a normal placenta, do arise from the edge of the chorionic plate. The description "haemorrhage

from the edge of the chorionic plate of the normally implanted placenta" though cumbersome, is anatomically correct. Appreciation of the frequency of this occurrence could lead to an improvement in our understanding and management of ante-partum haemorrhage. Instead of the single division of ante-partum haemorrhage into placenta praevia and accidental haemorrhage, which dates from the essay of Edward Rigby in 1776, cases of ante-partum haemorrhage could with advantage be segregated into (*a*) basal plate separation ("abruptio placentae"), (*b*) haemorrhage from the edge of the chorionic plate and (*c*) placenta praevia. In most cases haemorrhage of the first type can be readily recognized clinically. The real clinical difficulty is to distinguish between placenta praevia and haemorrhage from the edge of the chorionic plate of the normally implanted placenta.

From reviewing these 18 case records it appears that, until the later stages of pregnancy when physical and radiological signs become of value in the diagnosis of placenta praevia, there is no way of differentiating between haemorrhage from the edge of the chorionic plate and that due to placenta praevia.

If and when placenta praevia has been excluded with confidence, is it safe to allow these patients home? Although haemorrhage associated with placenta extrachorialis may recur and may be quite considerable, it appears that such haemorrhage from the edge of the normally situated chorionic plate carries little risk to mother or child. It would seem therefore, that in these cases a prolonged antenatal stay in hospital can be avoided with safety—*once placenta praevia has been confidently excluded.*

Aetiology of Placenta Extrachorialis

The theories of aetiology are many and none seems to be entirely acceptable. In the course of this study 4 placentae extrachoriales were found in women who had previously delivered similar placentae. The accuracy of the diagnosis in previous deliveries is open to considerable error but, as the basic incidence is as high as 18 per cent, this finding does not suggest the operation of a recurrent factor.

(1) *Implantation in the Cornual Region of the Uterus*

Hunter suggested that this was the explanation of the placental abnormality though he had never had the opportunity to test it by examining a placenta still attached to the uterus. Bayer (1910) advanced the same explanation in his "Tubenecke Placenta" theory. Torpin (1932) originally supported this idea but later (1953, 1955a, 1955c) opposed it. He personally found circumvallate placentae *in situ* on the anterior and posterior uterine walls as did Mattingly (1939). Torpin (1953, 1955b) also investigated placental situations by his amniotic sac distension method (Torpin, 1938), and found that 25 per cent of anterior or posterior uterine wall implantations were placentae extrachoriales.

Two specimens of extrachorial placentae *in situ* were obtained from the four intact gravid uteri and neither of these was attached at the uterine cornu (Fig. 3). Furthermore, if cornual implantations were an important factor in the aetiology of the condition, it would be expected that a high incidence of breech presentations would occur (Whitehead, 1953). In fact there was only a 3·1 per cent incidence (18 cases) of breech presentation in the series reviewed, the incidence for all deliveries being 4·2 per cent.

(2) *Endometrial Inflammation Theory*

This theory, of Veit (1885), is now outmoded by the realization that true inflammation of the endometrium is rare. Inflammatory changes are not found histologically.

(3) *Excessive Decidual Proliferation*

Successful placentation is dependent upon a proper balance being established between the invasive chorionic villi and the protective decidua. It is possible that excessive proliferation by the decidua round the margin of the young placenta might actively restrict the area of the chorionic plate. Such an idea was postulated by Schwab (1895) and is supported by the finding of decidual tissue in the circumvallate fold. Decidua, however, is not always present in the fold while, as Pinkerton (1956) pointed out, some of the folds are composed of chorionic tissue.

(4) *Folding of the Foetal Membranes*

Liepmann (1906) described four uteri in which undisturbed placentae had crescentic folds of membrane overlapping their margins. He ascribed these folds to variations in the amniotic fluid pressure relative to the growth and motility of the uterine wall. Such an explanation can only account for partial degrees of placenta circumvallata—it does not explain why the fold sometimes consists of more than membrane and why restriction of the chorionic plate can occur without the presence of a membranous fold.

(5) *Inco-ordination of Placental and Uterine Growth*

This idea is to some extent similar to the previous one. It was advocated by Sfameni (1908) and taken up in a modified form by Drosin (1935). It might be expected that disproportionate growth would have a shearing effect at the placental edge and result simply in separation with haemorrhage. While haemorrhage is a feature of many of these cases, in others there is no evidence of bleeding.

(6) *Compensatory Reduction of Chorion Frondosum*

Funck (1910) suggested that, if the area of placental chorion was excessive after the original atrophy of the chorion leeve at 8–12 weeks, a secondary atrophy of the peripheral part of the chorion frondosum might occur and produce the anomaly. This is quite incompatible with the facts. Active chorionic villi are found outside the ring which may enclose a very small area (Fig. 5).

(7) *Deep Implantation of the Ovum in the Decidua*

This idea was recently advanced by Torpin. His thesis is that if the ovum is deeply embedded in the decidua, the original placenta covers more than half of the early ovular sac, a ring forms at the placental edge and the membranes herniate through this to give the circumvallate placenta. If the implantation is less deep the result is a marginate placenta (Torpin, 1955a, 1955c). If this theory were true, it might be expected that there would be a high incidence of the anomaly in cases with a thick decidua. Torpin (1953) indeed shows a picture of an early circumvallate placenta *in utero* where the decidua is apparently extremely hyperplastic.

It is likely that the thickness of decidua in early pregnancy is related to the thickness of the endometrium at the end of a non-fertile cycle. Whether women who normally develop hyperplastic endometrium necessarily have a heavy menstrual loss, is not established but the patients who produced extrachorial placentae were all questioned as to their menstrual history.

The results were as follows:

Normal menstrual history	497 (86 per cent)
History of heavy menstrual losses (over 12 pads per period) *or* history of *irregular menses—sometimes* associated with heavy losses	81 (14 per cent)

A control series of 200 women whose placentae were normal, were similarly questioned. The same standards were applied and the results were as follows:

Normal menstrual history	156 (78 per cent)
Abnormal menstrual history as above	44 (22 per cent)

It will be seen that the incidence of abnormal menstrual loss is higher in the control group and, therefore, this provides no evidence to support Torpin's hypothesis. This finding should not, however, be regarded as evidence against his theory, for it is a study of an indirect nature. It may be wrong to assume that thick endometrium is associated with a heavy menstrual loss.

(8) *Superficial Implantation of the Ovum*

Nesbitt (1959) recently put forward an opposite view, namely that the cause is superficial rather than deep implantation. This, he argues, causes a small chorionic plate (see 10, below).

(9) *Splitting of the Decidua Vera*

Herff (1896) suggested that splitting of the decidua vera by the peripheral chorionic villi, resulted in the anomaly. Hamilton and Boyd (1951) state that such decidual splitting at the placental edge occurs normally, though to a

variable extent. Whitridge Williams favoured a combination of this idea and the next.

(10) *Initial Formation of an Excessively Small Chorionic Plate*

Williams's idea was that, if chorionic atrophy occurred initially over an excessive area giving a small chorionic plate, later the villi at the periphery would grow laterally to provide for the increased needs of the foetus. This idea is at variance with the present concept that the placenta normally continues to grow in area throughout pregnancy (Stieve, 1940; Hamilton and Boyd, 1951). In special circumstances, where excessive placental growth occurs, such as hydrops foetalis and severe erythroblastosis (Scott, 1958; Crawford, 1959), there is no particular tendency for the development of placenta extrachorialis. Out of 39 placentae from such cases personally examined, only 6 (18·2 per cent) showed any degree of placenta extrachorialis while only 6 of the 578 placentae extrachoriales (1·0 per cent) were associated with haemolytic disease. The control figure for haemolytic disease associated with "normal" placentae was 29 out of 2,583 (1·1 per cent).

Also, both this theory and that of "Compensatory reduction of the chorion frondosum" are made unlikely by the present finding of an approximately equal incidence of placenta extrachorialis in the second as in the last trimester of pregnancy.

(11) *Haemorrhage at the Placental Edge*

Pinkerton (1956) favours the view that the condition is the result of haemorrhage round the placental edge, occurring at an early stage of pregnancy. That such circumferential haemorrhages occur in extrachorial placentae and that they have a profound effect on the placental anatomy, was confirmed in the present study. It is, however, hard to conceive that they are of *primary* aetiological importance because many of the placentae, especially those of marginate type, show no evidence of haemorrhage.

(12) *Rupture of the Decidua Capsularis*

This idea was put forward by Lahm in 1924. He suggested that the decidua capsularis ruptures and retracts to form a collar which then restricts the chorionic plate (placenta marginata) and may sometimes lead to infolding of the membranes (placenta circumvallata). Williams dismisses this theory on the grounds that remnants of decidual tissue may be found outside the chorion laeve and separating it from that part of the placenta which is extrachorial. This would not seem a valid objection, however, as this might be decidua vera rather than encapsularis. This theory is attractive in that it explains all the anatomical features but it still awaits scientific proof.

Natural History of Placenta Extrachorialis and Mechanism of Bleeding

It is possible as a result of this study to postulate a sequence of events in the life of a placenta extrachorialis, though certain stages must be left to conjecture. At the outset, by some process unknown, the placenta is formed with the chorionic plate smaller than the decidual. This leads to a complete or partial placenta extrachorialis which may or may not have a membranous fold at the edge of the chorionic plate.

Given a placenta of this type there is a high risk that occult haemorrhage will occur from the edge of the chorionic plate, apparently due to a weakness of the encapsulating wall of the intervillous space. The extravasated blood, for some reason, travels round the edge of the chorionic plate, within the membranous fold if one is present. It may eventually form a complete ring of clot round the edge of the chorionic plate. This clot gradually converts to fibrin and retracts. Repeated haemorrhages of the same type may occur and give further layers of clot and fibrin. The contraction of the annular fibrin deposit frequently leads to further circumferential separation at a later date with more severe bleeding which results in clinical revealed haemorrhage (Fig. 16). The blood lost is maternal.

In the cases in which a considerable haemorrhage occurs, blood escapes from between the extrachorial placental tissue and the chorionic membrane and travels down between membrane and uterine wall to the cervix—the line of least

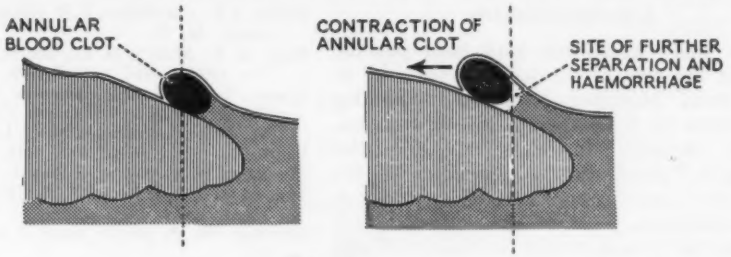


FIG. 16

Diagrammatic illustration of the probable mechanism of recurrent haemorrhage with placenta extrachorialis due to retraction of the ring of extrachorial blood clot or fibrin.

resistance. Thus the bleeding does not tend to lead to further placental separation as in abruptio placentae nor does it in any way interfere with the function of the placenta. This explains the fact that this type of ante-partum haemorrhage is relatively innocuous compared with abruptio placentae and placenta praevia. The whole placenta remains functional and so the baby is not at risk.

SUMMARY

(1) Placenta extrachorialis is a condition in which there is a complete or incomplete ring of placental tissue present outside the margin of the chorionic plate. The term covers circumvallate and marginate placentae but is to be preferred to these names for reasons given.

(2) There may be a membranous fold at the edge of the chorionic plate. This is primarily of chorionic membrane but amnion may also take part. The fold usually contains decidual tissue and frequently chorionic villi.

(3) A ring of blood clot or fibrin is frequently found at the edge of the chorionic plate and is situated within the membranous fold, if this is present.

(4) The aetiology of placenta extrachorialis is still unknown. The theories of its development are discussed.

(5) In a series of 3,161 consecutive placentae, the incidence of placenta extrachorialis was 18 per cent—approximately half of these showing extrachorial rings of haemorrhage.

(6) Placenta extrachorialis has no clinical significance for mother or foetus, unless it is complicated by an extrachorial ring of haemorrhage. It may then give rise to clinical haemorrhage of a type similar to that which occurs with placenta praevia. This association is statistically highly significant.

(7) The problems of diagnosis and management in these cases are discussed.

(8) It is postulated that, if a placenta is initially formed as a placenta extrachorialis, there is a tendency for minor bleeding to occur from the edge of the chorionic plate. This results in an annular clot or ring of fibrin, which on contraction may lead to further peripheral separation and bleeding with revealed haemorrhage.

(9) The relationship of this type of ante-partum haemorrhage to so-called "marginal sinus rupture" is discussed. There is little evidence in favour of the existence of the "marginal sinus" as an anatomical structure or to show that the marginal region of the placenta is physiologically important. Nevertheless, haemorrhage from the periphery of the normally implanted placenta is a definite clinical entity and one which occurs with increased frequency when the placenta is of extrachorial type. In all cases the haemorrhage originates from the edge of the chorionic plate and it is suggested that cases of ante-partum haemorrhage should be divided into (*a*) abruptio placentae, (*b*) haemorrhage from the edge of the chorionic plate and (*c*) placenta praevia.

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LYMPHATICS OF THE VULVA

BY

E. PARRY-JONES, M.D., M.S., M.R.C.O.G.
Consultant Obstetrician and Gynaecologist
H. M. Stanley Hospital, St. Asaph

INTRODUCTION

ONE of the more unpleasant sights that a gynaecologist has to face is that of a vulvectomy operation where the excised area is left unsutured. It has been stated by some with much experience of carcinoma of the vulva that this is unavoidable because a wide excision is essential in all cases. Nobody will deny that the incision should pass through healthy tissue but how wide should this incision be? Way (1951), who has done so much to improve the results of carcinoma of the vulva, is the pioneer of the ultra-radical approach to this disease. As far as his incisions are concerned their lateral boundaries, extending as they do on to the thigh, cannot be merely to have an incision which is far removed from the growth because an area is left around the urethra which may well be nearer the growth than the outer edge of the labium majus. Furthermore, the incision is wide on both sides irrespective of the site of the primary growth. The need of these incisions may not be immediately apparent but the answer is found in the anatomical and gynaecological textbooks.

The anatomists state and the gynaecologists quote that normally some of the lymphatics of the vulva pass on to the inner aspect of the thigh to reach their termination in the inguinal and femoral nodes. It would appear, therefore, that the purpose of these incisions is to remove, not only all the lymph nodes, but the lymph vessels as well. As the author doubted the anatomical statements he decided to re-investigate the lymphatics of the vulva to determine whether the work carried out by Sappey over 80 years ago and on which rests the modern concept of the vulval lymphatics, was indeed correct.

PREVIOUS INVESTIGATIONS OF THE LYMPHATIC SYSTEM OF THE VULVA

Neither Mascagni (1787), Fohmann (1833) nor any of the older anatomists investigated the vulval lymphatics. This honour was left to Sappey who, in 1874, described the lymphatics in the following terms:

"By their origin and disposition, as well as by their course and termination, these vessels present a remarkable analogue with those which occur in the external genital organs of the male. They both arise in the skin and in the adjacent mucosa but those which originate in the vaginal and urethral mucosa are sparse. It is only on the labia majora and minora that their density can be compared with that of the scrotum.

"These vulval vessels arise, as throughout the cutaneous covering, in the papillae which are as dense as those in the glans. The minute branches provided by these vessels anastomose with each other in the sub-papillary bed forming an extremely fine network which is super-imposed in several layers. This network covers the fourchette, the urethral orifice, the clitoris, the labia minora and the medial surface of the labia majora; it is so loose and closely interwoven in all parts that when it has been well injected it presents an ashy grey appearance, and it is necessary to use a magnifying glass to distinguish the innumerable silvery filaments of which it is composed. On the lateral surface of the labia majora the network is composed of larger branches which can be distinguished by the naked eye.

"*From the periphery of this profuse network a large number of trunks arise which take different directions* (*Fig. 1*). *Those which come from the*

antero-superior part of the vulva travel more or less vertically before inclining to the right or left in long arcs whose concavity is inferior. They terminate in the superior inguinal glands. The others go forward and outwards in the fold between the vulva and the thigh to terminate in one or two glands below the preceding ones. The trunks which arise from the posterior part of the vulval ring travel forwards on the inner aspect of the thigh immediately outside the vulvocrural fold to end in the inferior inguinal glands. They are accompanied by the trunks which come from the perineum and the anal region and which terminate in the same group of glands."

Bruhns (1898) demonstrated the general intercommunication of the capillaries of the labia majora and minora and emphasized the contralateral connexions of the vulval lymphatics.

He drew attention to the difficulties associated with the investigation of Bartholin's gland and was not able to confirm that the lymphatics of the gland went to the pelvic lymph nodes as believed by Huguier, Martin, Leger and Tarnier, nor that they went to the inguinal nodes as believed by Bonnet.

Cunéo and Marcille (1901) demonstrated that the lymph drainage of the clitoris varied according to its origin. That from the prepuce went to the superficial inguinal nodes whereas those from the glans went along the dorsum of the clitoris to reach the front of the symphysis before going to the deeper glands.

Poirier (1903), who was one of Sappey's pupils, repeated Sappey's description without adding anything new.

Neither Tandler (1926) nor Rouvière (1932) had any further information to add to the knowledge of vulval lymphatics.

Crossen and Crossen (1948) have repeated Poirier's description in all editions of their book from 1915 onwards. Way (1951) described the vulval lymphatics, supporting the descriptions already given. Only Shaw (1954) put forward a slight modification of the accepted statement and although he did not quote his source it is probable that he took Bruhns (1898) as his authority.

These opinions have been put forward by anatomists and accepted by most gynaecologists and although it is not denied that the superficial lymphatics drain into the inguinal and femoral nodes nor that contralateral connexions may exist reasons will be put forward why it does not appear reasonable that the lymphatics normally pass on to the thigh to reach their terminal nodes.

Reasons for Doubting the Present Concept of the Superficial Lymphatics

The male homologue of the labium majus is the scrotum and the skin covering it is drained by vessels which, together with those of the perineal skin, pass along the course of the external pudendal blood vessels to the superficial inguinal lymph glands. Sappey (1874) depicts the lymphatic drainage of the scrotum and perineum as passing along the groove between the scrotum and the thigh (Fig. 2).

As the labium majus is also supplied by the external pudendal vessels it would be expected that the lymph vessels would follow them rather than embark on any other course.

Furthermore, the vulva is peculiar in that it is continuous with the adjacent skin but developmentally it has no connexion with it. Nowhere else on the female body is a similar circumstance to be found. For most of the body surface, the lymphatic trunks drain into their regional nodes by the shortest route. This is true of the leg, arm, chest, abdomen, head and neck and also the breast.

The fact that Poirier, when describing Sappey's method, states "It goes without saying that the injection (of mercury) should always be made in the direction of the current of lymph" indicates that the injection was not really for the purpose of investigation but to confirm what was already thought to be a fact. The possibility of error and the production of artefacts has to be seriously considered, when it is appreciated that to undertake the injection: "First of all an adult subject, and one as thin as possible should be chosen. If putrefaction is so advanced that the skin is green and the epidermis raised in large flakes, the injection of the cutaneous lymphatics is favoured" (Poirier).

The post-mortem injection of mercury involves a certain amount of pressure. This, combined with the particular difficulties associ-

FIG. 1
Origin and course of vulval and perineal lymphatics (Sappey, 1874).

FIG. 2
Origin and course of scrotal and perineal lymphatics (Sappey, 1874).

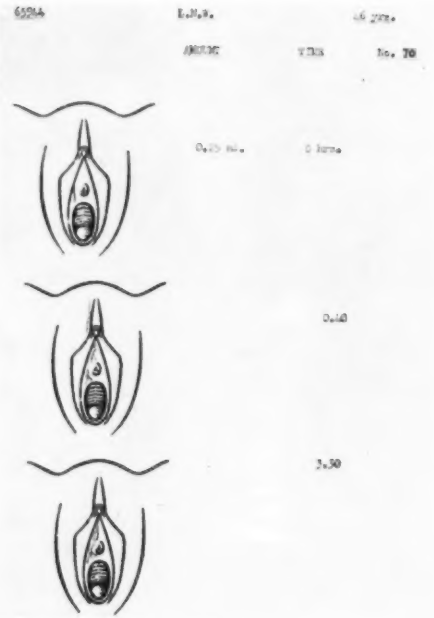

FIG. 4
Vestibule.

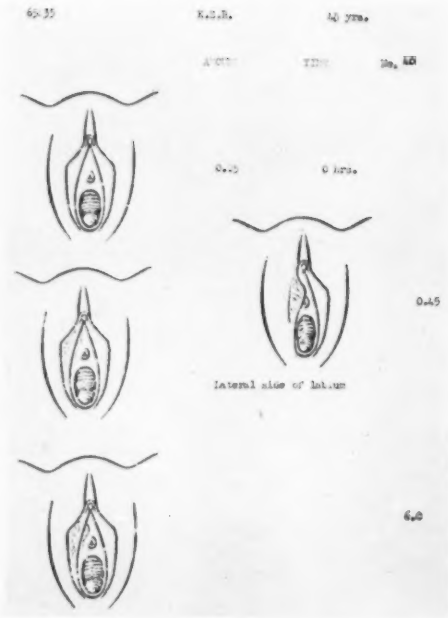

FIG. 5
Labium minus.

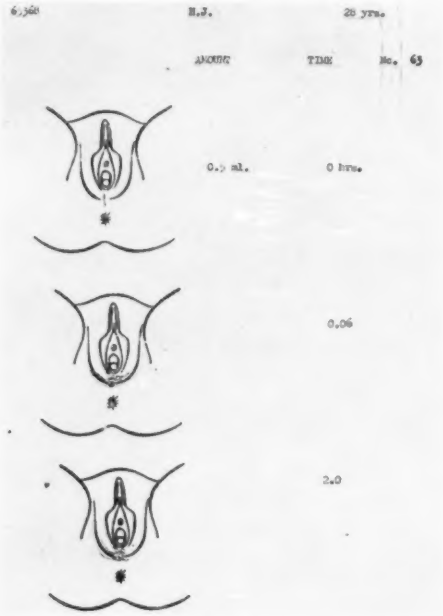

FIG. 6
Perineum.

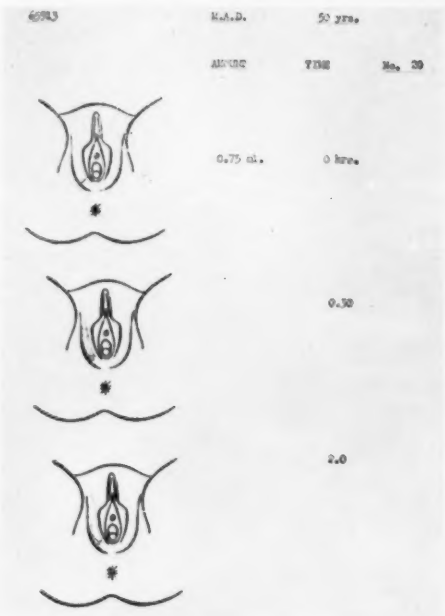

FIG. 7
Labium majus.

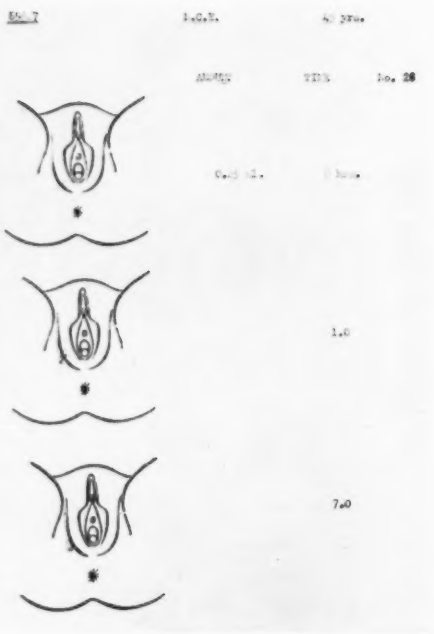

FIG. 8
Labium majus.

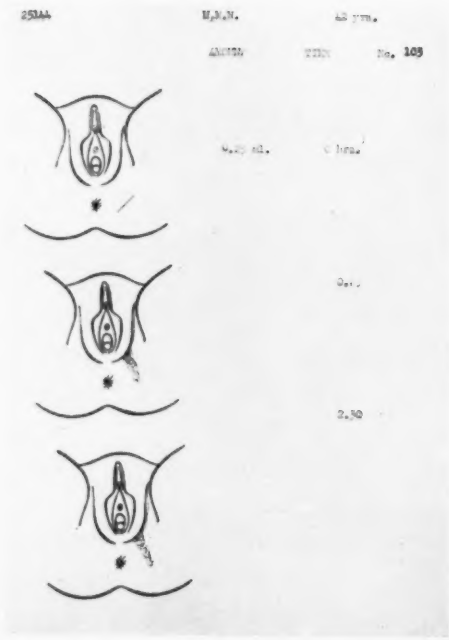

FIG. 9
Skin adjacent to vulva.

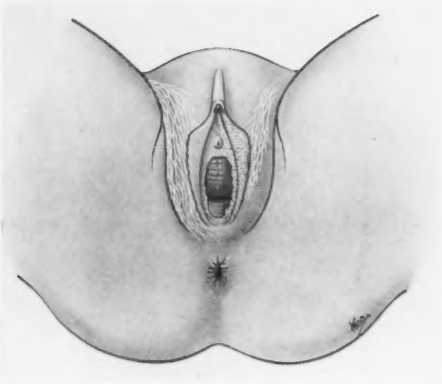

FIG. 10

Lymphatic drainage of labium majus and labium minus (medial surface).

FIG. 11

Lymphatic drainage of vestibule, labium minus (lateral surface), perineum, and skin adjacent to vulva.

ated with the vulva, namely, its relatively small size, curved shape and irregular surface, make it almost impossible to avoid the effect of gravity. These factors may well result in the opening of lymphatic channels which do not normally belong to the vulva.

Re-investigation of the Vulval Lymphatics

The investigation of the lymphatics of any organ must take into account its development and its blood supply for these determine its lymphatic drainage (Sabin, 1902; Huntington, 1911).

Development of the Vulva

Initially the precursor of the vulva commences on the ventral aspect of the embryo and later moves during development into its adult position (Hamilton, Boyd and Mossman, 1944).

During these early stages the limb buds project laterally. Their development and alteration in position coincides with that of the vulva and explains the distribution and course of the blood supply to the external surface of the vulva.

Blood Supply of the Vulva (Fig. 3)

The blood supply of the vulva comes from:

(*a*) Femoral artery *via* superficial and deep external pudendal.

(*b*) Internal iliac artery *via* internal pudendal.

The veins travel back alongside the arteries.

It will be observed that the blood supply of the vulva arises from two main sources. The superficial and deep external pudendal which supply the more superficial part of the vulva and the internal pudendal which supplies the deeper layers of the vulva.

Demonstration of the Vulval Lymphatics

(1) *Choice of Substance for Investigating the Vulval Lymphatics*

As all the previous work on the vulva had been carried out post-mortem it appeared advantageous to investigate the lymphatics *in vivo*, so that the methods of Nuck (1697), Mascagni (1787), Fohmann (1833), Sappey (1874) and Gerota (1896) were not used. As the number of cases is small in which the entire vulva is removed at operation the method of Gray (1938) and others (using radio-opaque fluid) was unsuitable. Radioactive gold (Au 198) used by Bloom and Gregory (1958) in the investigation of the lymphatics in breast cancer showed that the radioactive scatter at the primary injection site overshadowed the relatively small uptake in the nearby nodes (only 10 per cent is absorbed by the lymphatics). A similar problem would obviously occur in the investigation of the course of the vulval lymphatics and so was not considered satisfactory.

Particulate dyes such as Indian ink and colloidal graphite were not used because of the permanent staining at the injection site which was considered undesirable.

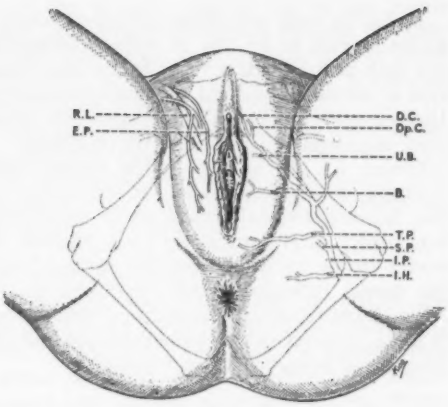

FIG. 3

Blood supply to the vulva (for the sake of clarity veins have been omitted).

Key to lettering:

R.L.	Round Ligament.
E.P.	External Pudendal Arteries.
D.C.	Dorsal Artery of Clitoris.
Dp.C.	Deep Artery of Clitoris.
U.B.	Urethral Branch.
B.	Artery of the Bulb.
T.P.	Transverse Perineal Artery.
S.P.	Superficial Perineal Artery.
I.P.	Internal Pudendal Artery.
I.H.	Interior Haemorrhoidal Artery.

By far the most promising method of investigation seemed to be that of using a diffusible dye such as Patent Blue V* or Evans Blue. This type of substance was first used with success by Hudack and McMaster (1933) and has been used extensively since by Kinmonth (1952).

Owing to the success which others had achieved with Patent Blue it was used in this investigation and found to be eminently satisfactory. It is particularly useful because it makes visible the local superficial network and the deeper collecting trunks. Furthermore, it has no known toxic effects, its rate of absorption is rapid, it leaves no permanent staining and its generalized body colouring is transient.

(2) *Method*

During this investigation Patent Blue V (11 per cent w/v) was used in amounts varying from 0·1 to 1·0 ml. The larger amounts were injected in the early part of the investigation until it was found that the smaller amounts showed up the superficial and deep lymphatics well and that the generalized body colouring was less. For most patients 0·5 ml. was the quantity used.

Varying sites were chosen and included the anterior, middle and posterior thirds of the labium majus, the labium minus, the vestibule, the clitoris and the perineum. The direction and extent of the injection varied but these had little, if any, effect on the lymphatic spread. As intradermal injections are intralymphatic (Kinmonth, 1952) they were used almost exclusively.

In addition to the above areas the inner aspect of the thigh was injected to ascertain whether the lymphatics adjacent to the vulva could be seen. If they were visible then it could be assumed that lymphatics passing from the vulva on to the thigh would also be seen.

There was no selection of patients. Every patient undergoing operative treatment, whether major or minor, was subjected to an injection of Patent Blue. They varied in age from 20 to 87 years and in build from thin to obese. The total number of injections was over 100.

* Obtainable from Savory & Moore, Ltd., London.

(3) *Technique*

The initial injection was made with the patient in the lithotomy position under general anaesthesia. The area was cleaned with spirit and a 14-gauge needle employed. To facilitate the injection the needle was bent at an angle of approximately 50°.

Following the technique of Kinmonth (1952), the needle was inserted, bevel down, to the required distance moving the point a little from side to side to disrupt the superficial lymphatics. The plunger of the syringe was pressed during the withdrawal of the needle. The injection was discontinued before the complete withdrawal of the needle to avoid spill. If this occurred in spite of care the dye was removed with spirit to avoid any artificial skin colouring. On completion of the injection the area was rubbed vigorously to aid the intralymphatic absorption of the dye.

The minor or major operation was then carried out. The injection site was examined during the operation and immediately prior to the patient's removal from the theatre and at frequent intervals after her return to bed. The findings were recorded diagrammatically.

Within a few moments of the intradermal injection fine blue tendrils (0·2 cm.–0·8 cm.) appeared radiating from the injection site. These soon became obscured by the generalized spread of the dye over an area of variable size and shape depending on its situation, the greater part of which was usually formed by the spread of the dye in one direction.

After a delay of half a minute or more, the deeper trunks became visible. Occasionally during an injection, a blue line would appear only to disappear equally quickly, indicating that a blood vessel had been punctured.

In order to test whether visual examination of the skin gave a true picture of the lymphatic spread, in two cases the dye was injected into the vulva prior to vulvectomy for carcinoma. Post-operative dissection confirmed the visual findings.

AREAS INVESTIGATED

(1) Clitoris.
(2) Vestibule.

(3) Labium minus: medial surface; lateral surface.

(4) Perineum.

(5) Labium majus: anterior, middle and posterior thirds.

(6) Skin adjacent to the vulva.

(1) *Clitoris*

The investigation of the clitoris was difficult and the only conclusion reached was that the lymphatic network of the prepuce is evenly spread over its surface. It was not possible to observe the course of the deeper trunks which disappeared into the substance of the mons.

(2) *Vestibule* (Fig. 4)

The injections were made anterior, lateral and posterior to the urethral orifice.

The drainage from all the anterior and most of the posterior part of the vestibule went alongside the clitoris. The vessels disappeared under the anterior part of the labium minus to appear in the groove lateral to the clitoris. The trunks from the posterior part of the vestibule either passed under the posterior part of the labium minus or curved round its posterior margin if the labium was small. From there it either passed on to the labium majus or into the interlabial groove.

Where the injection was para-urethral there was spread anteriorly across the midline.

(3) *Labium Minus* (Fig. 5)

The injections for the labium minus were made along the medial and lateral surfaces and in the interlabial groove.

On the medial side the lymphatics spread down the labium to its base. In many cases they extended on to the vestibule to reach the para-urethral area but the spread only went as far as the midline.

Those lymphatics in the most anterior part of the labium moved directly anterior whereas those nearer the centre moved to the base of the labium before turning anteriorly to join the other trunks. Together they disappeared under the most anterior part of the labium to reappear laterally to the clitoris, only to disappear again into the substance of the mons.

In the posterior part of the labium minus when the lymphatic vessels reached the base of the labium they disappeared to present themselves on the labium majus whose lymphatics they joined to travel anteriorly.

On the lateral surface of the labium the lymphatics remain on the lateral side and either join the trunks of the labium majus or pass anteriorly in the interlabial groove to reach the lateral side of the clitoris.

(4) *Perineum* (Fig. 6)

The injections were made in vertical and horizontal directions. When sited transversely just anterior to the anus there was a generalized spread in all directions. Initially, the trunks passed laterally then coursed round the labium majus towards the junction of the thigh and the mons veneris.

In some cases, when the injection was made vertically, the dye spread on to the vulva. The subsequent course of the lymphatics was the same as in the labium majus.

(5) *Labium Majus* (Figs. 7 and 8)

The injections were made into all parts of the labium majus and in all directions. On occasion the injection deliberately included an area outside the vulva.

In the anterior third the dye spread anterior to the injection site in a very limited degree; definite trunks were only occasionally seen and then for a very short distance.

In the middle and posterior third the density of the network was much greater than in the anterior third. The spread was almost entirely in an anterior direction and in all cases what lateral spread there was, was arrested at the labio-crural fold. All the lymphatic trunks travelled anteriorly and had no tendency to travel in any other direction.

The demarcation of the posterior third was not easy in all cases owing to the alteration in the normal anatomy following parturition but even in these cases the basic points were constant.

The lymphatics travelled in an anterior direction following the line of the labium majus. In a few cases there was a tendency for them to split into two main groups as they travelled

forwards so that they appeared on both sides of the labium with a comparatively free area between them.

The trunks travelled along the length of the labium to disappear into the infero-lateral part of the mons veneris. The lateral spread of the dye was arrested in all cases at the labio-crural fold.

In those cases where the injection deliberately included an area outside the vulva the trunks took a curved course towards the labio-crural fold which they joined or nearly joined more anteriorly.

(6) *Skin Adjacent to the Vulva* (Fig. 9)

The reasons for including this area have already been explained (page 922, paragraph 5).

The injection sites, on the inner aspect of the thigh, varied in position from the most anterior to the most posterior part which was visible with the patient in the lithotomy position.

Irrespective of the site of the injection the spread of the superficial lymphatic went medially or antero-medially as far as the labio-crural fold and no farther. There was a distinct line of demarcation at the junction of the labium majus and the adjacent skin—a similar line to that which was found when the labium majus was injected.

Apart from the spread of the superficial lymphatic the trunks also went towards or into the labio-crural fold which they joined at a varying point depending on whether the injection was more posterior or less.

There was no tendency for the trunks to pass laterally. Only when the injection was well out on the thigh did the trunks cross over the thigh at a point lower than the junction of the thigh and mons veneris.

Discussion

It is only in comparatively recent years that the treatment of carcinoma of the vulva suggested by Basset (1912), Kehrer (1912) and Stoeckel (1930) has been adopted by most gynaecologists. Taussig (1931) and Way (1948) are largely responsible for the present day approach to this disease. Previously, treatment consisted of local removal of the growth, local vulvectomy, coagulation diathermy, radiotherapy and hemivulvectomy with or without lymphadenectomy.

The results of these various treatments reported over the years leave no doubt that the best main modern attack is surgical and that this must consist of vulvectomy and bilateral lymphadenectomy. More recently Way (1954) has lent support to Taussig's (1931) opinion regarding the inadvisability of removing the deep glands in all cases. This need not be enlarged upon here. Suffice it to say that the appreciation of the necessity to remove the lymph nodes on both sides in addition to the vulva has greatly improved the prognosis of this disease. The problem now is to decide in what way the results may be improved.

Avoidance of Mortality and Morbidity as a Result of Sepsis

One of the most serious complications of vulvectomy operations is that of wound sepsis and is the most important single cause of post-operative deaths (Way, 1951). Some surgeons claim that it always occurs (McKelvey, 1947) and others that healing is rarely by first intention. Antibiotics and various local applications have made but little difference and Way and McKelvey have had no success with immediate skin grafting.

Infection of the wound arises from two main causes; first, the proximity of the operation field to the anus and the vagina, as neither of them can be completely sterilized, second, the open wound invites sepsis. Although little can be done to influence the effect of the first cause, the second offers a challenge. Indeed, it is in this direction that one of the chances of improving the results may lie. If this problem of sepsis can be avoided or reduced then there will be an improvement not only in the more obvious matter of post-operative deaths but also in the degree of pain and discomfort which follows in the wake of an infected wound.

In some cases a wide excision *has* to be performed in order to ensure that all carcinomatous tissue is removed. Indeed, Way advises this wide excision in all cases and maintains that if it is possible to close the vulval wound the operation has not been complete. This view is not shared

by Cosbie (1952), Marshall (1953), Shaw (1954), Arthure (1958) and others but has profoundly affected the present-day opinion on the extent of the incisions in carcinoma of the vulva in this country and abroad.

The basis of Way's (1951) recommendation is founded on the work started by Sappey (1874) who maintained that many of the superficial lymphatics of the vulva passed to the inguinal and femoral region by way of the thigh. In order to remove all the lymphatic vessels it was thought necessary to excise the vulva by making the incision along the inner aspect of the thigh (Fig. 12).

It has been shown by this present investigation that at no point do the vulval lymphatics cross the labio-crural fold to reach the inguinal and femoral nodes. Only from the perineum do the lymphatics skirt round the vulva rather than travel up the labium majus. It might be argued that these findings are those of normality and are not valid in disease. Nevertheless, it can be stated that in two cases of carcinoma of the vulva where injections of dye were employed the findings were confirmed, i.e., the dye did not spread on to the thigh (Fig. 4 a and b). Furthermore, as the modern operation for carcinoma of the vulva has been based on Sappey's teaching of the vulval lymphatics, it would appear not unreasonable to alter the surgical approach in accordance with the newly-acquired knowledge. Indeed, it is well known that many surgeons for many years have chosen to restrict their incisions to the vulval boundary rather than employ the extra wide incisions advised by Way (1951).

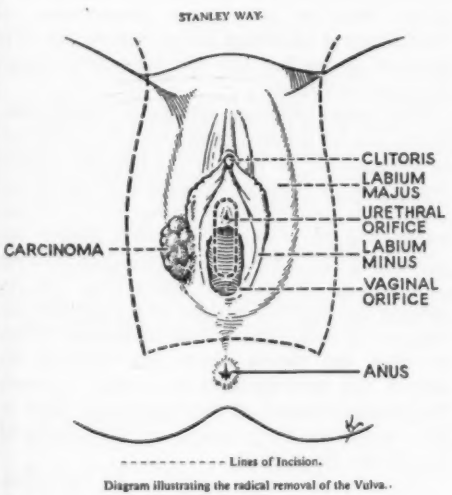

FIG. 12

Way's incisions for removal of the vulva in carcinoma (Way, 1951, p. 38).

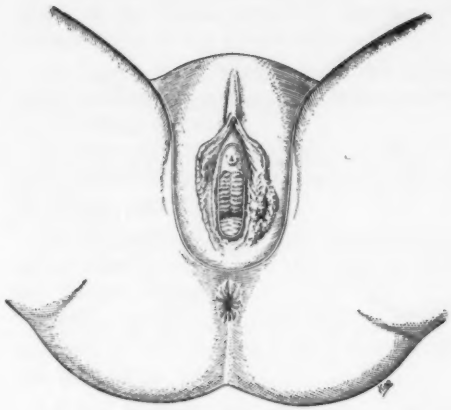

FIG. 13

Recommended incisions for removal of vulva.

The author believes that the need for an incision which extends beyond the confines of the vulva should be avoided except in cases where growth approaches the labio-crural fold or involves the perineum. Support to this statement is obtained from the clinically observed fact that a secondary carcinoma on the medial aspect of the thigh does not occur and the direct spread of the primary on to the thigh is late.

The restriction of the vulval incisions to its boundaries (Fig. 13) enables the wound to be closed without tension in most cases. To achieve this, attention must be paid to the method of closure (Fig. 14). The groin incisions are similar to those used by Way (Fig. 15), the only difference being that the medial incision of the V goes to the top of the thigh. The author employed these incisions in the last 7 cases of

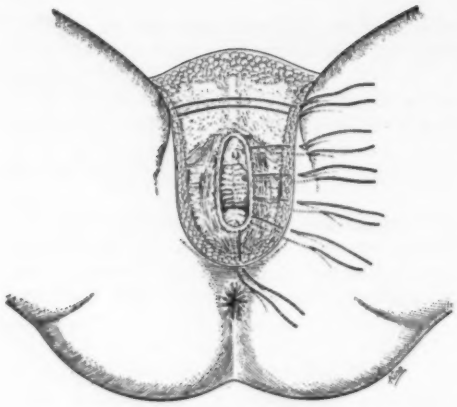

FIG. 14

Method of closure. All sutures are inserted and closure is deferred until the patient is moved up the operating table and her legs extended and partially adducted.

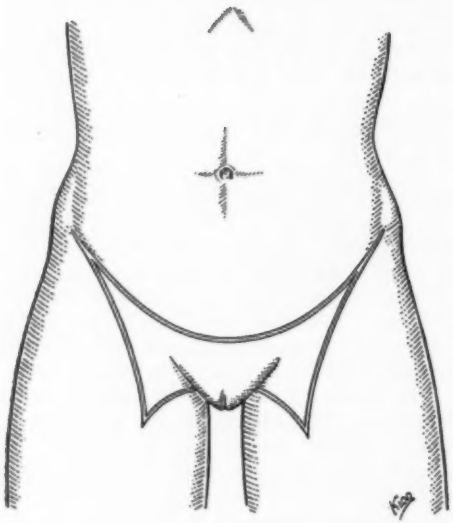

FIG. 15

Groin incisions. Note that medial branch of V incisions goes to the top of the thigh.

carcinoma of the vulva and the vulval wound healed by first intention within two weeks in 6 cases. The remaining case died of coronary thrombosis within 6 hours of the operation.

The advantages which accrue from primary closure of the wound are:

(1) The amount of serous discharge is greatly minimized so that the problem of disturbed blood chemistry is avoided.
(2) The amount of nursing attention required is much less.
(3) The patient is more comfortable and is disturbed less often for the renewal of dressings.
(4) Sepsis is avoided.
(5) The duration of hospitalization is reduced.
(6) The incidence of recurrence is not affected (Cosbie, 1952).

Contrary to the practice of some surgeons (Collins *et al.*, 1956; Martius, 1957) it is imperative that the entire mons veneris be removed in all cases because it is through this area that all the lymphatics pass during some part of their course to reach the inguinal region. Way maintains that carcinoma of the vulva spreads to distant points by emboli along the lymphatics rather than by permeation. Nevertheless, it would appear advantageous to remove not only involved nodes but also the lymphatic trunks draining into them.

The present technique for the internal incision is to skirt the urethral orifice on either side and to cross above the level of the hymen to incise the vagina. In view of the ease with which the lymphatics communicate between the labium minus and the vestibule it would appear advisable, in cases where the carcinoma involves or arises in the labium minus (Fig. 16), to remove the terminal portion of the urethra and adjacent tissues. This entails an incision which encircles the vagina above the level of the hymen and goes through the urethra to reach the inferior border of the symphysis. Only in this way can the removal of all superficial lymphatics be ensured.

The extended radial operation for carcinoma of the vulva has been based on the principle that the lymphatic drainage of the vulva goes to the superficial and deep inguinal and femoral nodes

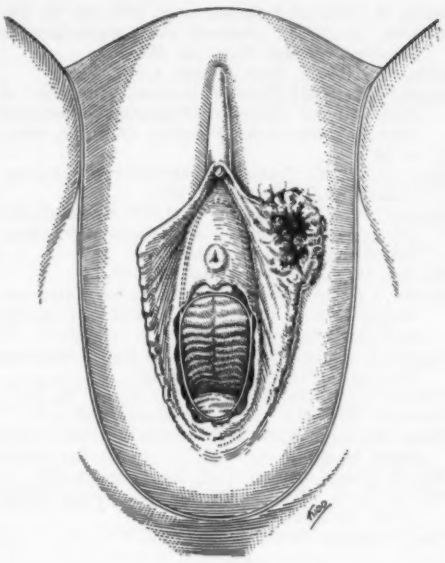

FIG. 16

Recommended incision when growth involves labium minus. Dotted line indicates extension of incision through lower urethra to lower border of symphysis pubis.

The correctness of this assumption has been proved by the excellent results which have been obtained from the operation by Taussig (1940, 1941) and Way (1951) and others. Nevertheless, the knowledge regarding the superficial lymphatics has been incomplete and inaccurate and the more complete knowledge which this investigation has provided makes it possible to alter the surgical approach in a few details which results in a shorter convalescence and may well produce an improved recurrence rate.

SUMMARY

(1) Lymphatic vessels from the vulva do not cross the labio-crural fold at any point to reach their termination in the inguinal and femoral nodes.

(2) The lymphatics of the labium majus travel along the length of the labium.

(3) Lymph flows readily from the labium minus to the labium majus but not from the labium majus to the labium minus.

(4) Lymph flows readily from the labium minus to the vestibule but not from the vestibule to the labium minus.

(5) The lymphatics from the vestibule go alongside the clitoris or to the posterior part of the labium majus.

(6) The lymphatics from the perineum travel either immediately outside the vulva or along the labium majus.

(7) The lymphatics of the skin immediately adjacent to the vulva go into or parallel with the labio-crural fold.

(8) No evidence was seen for or against contralateral or retrograde spread.

(9) The findings of the investigation confirm that the operation for carcinoma of the vulva should consist of inguinal and femoral lymphadenectomy together with vulvectomy. The vulvectomy incision should skirt the vulval boundary except in cases where the growth encroaches on the labio-crural fold or involves the perineum.

(10) The lower portion of the urethra should be removed not only when it is involved by growth but also when the growth involves the labium minus.

(11) Primary closure of the wound is possible in most cases and the benefits of this are put forward.

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THE PELVIC LYMPHOCYST

BY

W. G. MILLS, F.R.C.S., F.R.C.O.G.

Gynaecologist

United Birmingham Hospitals

THE dissection of lymphatic vessels and nodes from the lateral wall of the pelvis has become a recognized part of the surgical treatment of carcinoma of the cervix and, to a lesser extent, that of carcinoma of the uterine corpus and carcinoma of the vulva. Many such lymphadenectomies have been performed without complication other than the occasional production of severe venous haemorrhage and few, if any, symptoms of lymphatic obstruction have arisen. However, reports from Japan (Kobayashi and Inone, 1950; Mori, 1955) and more recently from America (Gray *et al.*, 1958; Rutledge *et al.*, 1959; Nelson and Husten, 1959) have described a sequel of these operations in which a lymphatic cyst may develop at the site of operation and enlarge upwards into the lower abdomen. The condition has been given the name of "Lymphocyst" and, although it appears to run a benign course with few symptoms, its discovery during routine follow-up of these patients must occasion some alarm unless its true nature be realized.

The incidence of the condition varies greatly. Mori (1955) reports it in 48 per cent of cases and Rutledge *et al.* (1959) in 24 per cent, but Meigs (1954) does not even mention the complication despite his vast experience of radical pelvic surgery. Two cases have been found in a personal series of 90 pelvic lymphadenectomies for uterine cancer and these will be briefly reported.

CASE REPORTS

Case 1

Mrs. F.M. was seen at the age of 57, ten years after the menopause, as a nullipara with post-menopausal bleeding. Curettage confirmed adenocarcinoma of the corpus uteri and she was treated on 12th December, 1952, by hysterectomy with removal of the uterine appendages and bilateral pelvic lymphadenectomy. The pathological report showed no malignancy in the excised lymph nodes.

In May, 1953 there was slight bleeding from the vaginal vault and although biopsy was negative she was irradiated with vaginal radium.

In May, 1954 routine examination disclosed for the first time a smooth cystic tumour arising from the left side of the pelvis and extending into the lower abdomen. Operation on the 14th June showed it to be an extraperitoneal elongated cyst, about 18 cm. deep and some 10 cm. broad. The wall was thin and it contained clear yellow fluid. It was followed to a point below the bifurcation of the common iliac artery, but the excision was incomplete and the wound was drained.

Four months later the cyst had recurred exactly as before. Aspiration removed 250 ml. of yellow fluid which contained a few leucocytes. The cyst rapidly refilled and within a month it had returned to its original size, but as it caused no symptoms operation was delayed for 5 months.

On 29th April, 1955, a second attempt was made to remove it. Dense adhesions were separated from the posterior rectus sheath, a litre of yellow fluid was aspirated and an arduous extra-peritoneal dissection performed; the level of the ischial spine was reached, the bladder was inadvertently opened and still a small residual portion of the cyst remained very deep in the pelvis. This was freely carbolized with pure phenol and the wound closed. Dr. C. W. Taylor reported that the specimen showed laminated connective tissue with scattered lymphoid elements and no epithelial lining. The fluid showed albumin (+++), urea 0·1 per cent and occasional lymphocytes. The patient returned home.

Within 2 months the mass had returned and was the size of a 20-weeks gestation. It remained unchanged for 11 months causing no symptoms and the patient then refused to return for further examination. She was eventually examined at home on 17th November, 1958, almost 6 years after her original operation, and no evidence could be found of any cyst nor of any recurrent tumour.

Case 2

Mrs. A.R., aged 58 and with 3 children, was seen with post-menopausal bleeding. Curettage confirmed an early

adenocarcinoma of the endometrium and it was treated in the first place by insertion of 50 mg. tube of radium into the uterus for 5 days. On 18th August, 1958 a Wertheim operation was performed with bilateral pelvic lymphadenectomy. The specimen showed that the growth had been almost entirely destroyed by the radium and there was no malignancy in the lymph nodes.

Three months later she was well and free from disease, but in February, 1959 routine examination showed a tumour in the right inguinal region, palpable bimanually and apparently fixed to the pelvic brim. A month later it was definitely larger, but still quite painless, suggesting a grossly enlarged lymph node arising from the obturator fossa. At operation on 16th April, 1959 it was exposed through a muscle cutting inguinal incision and proved to be a tense cyst full of clear yellow fluid, fixed extra-peritoneally to the pelvic wall deep to the external iliac vessels. It was completely removed and reported as consisting of laminated connective tissue with scattered lymphocytes. In December, 1959 there was no sign of recurrence.

Discussion

Reference to the American and Japanese literature quoted above suggests that these two cases are examples of the condition designated "Lymphocyst", in which an extra-peritoneal cyst appears to develop from some lymphatic source following lymphadenectomy in the pelvis. The benign course devoid of symptoms seems characteristic, as is the spontaneous regression of the larger cyst following unsuccessful attempts at surgical removal. By far the most serious feature of the condition is the natural anxiety of the doctor responsible for the follow-up of the patient that it might represent some recurrence of the malignancy. This could well lead to unnecessary and dangerous courses of pelvic irradiation, without surgical exploration and biopsy to determine the true nature of the cyst.

The cause remains obscure. Mori (1955), who recorded the condition in almost half of his patients subjected to lymphadenectomy, found a correlation between the incidence of lymphocyst and the number of nodes removed. Rutledge *et al.* (1959) with an incidence of 24 per cent considered such factors as the stage of the carcinoma, the employment of post-operative irradiation and the occurrence of nodal metastasis, but could find no significant association. The two cases recorded have followed operations which have certainly not been carried out with the meticulous dissection performed by some gynaecologists. It is perhaps significant that an association between lymphatics and the peritoneum seems to be necessary, for the condition does not appear to have been described following dissection of lymphatics of the axilla or of the neck.

The exact nature of the lymphocyst is uncertain. Rutledge *et al.* (1959) state that the fluid content of the cyst is not static and that it should be regarded as a reservoir with a steady stream of fluid passing through. This will explain the rapidity with which it refills after aspiration, and perhaps the tendency towards recurrence after incomplete excision, but it is still hard to envisage the mechanism whereby the cyst wall can reform within a few weeks of its subtotal excision. It may be conjectured that it represents a sub-peritoneal lymphatic space that becomes flooded by fluid whose natural pathways have been excised or blocked by surgery, but this does little to explain the variations in incidence or the variability of the interval between operation and its development (from 10 days to 18 months).

The management of lymphocysts will depend to some extent upon the certainty with which the diagnosis can be made. Departments in which it is of common occurrence may well dispense with biopsy and treat the condition conservatively in the expectation of spontaneous resolution. Those with less experience will feel the need for biopsy and some form of active intervention. Repeated aspiration and drainage seems to lead to secondary infection with the production of deep abscesses. Rutledge *et al.* (1959) used intramuscular injections of trypsin with only partial success. Nelson (1959) treated his two cases by "unroofing" and this was probably successful in diverting the lymphatic flow from the cyst into the peritoneal cavity. A similar successful result might well have followed the operations on Case 1 (above) had they been conducted from within the peritoneal cavity rather than extra-peritoneally. It would therefore seem reasonable to attempt complete excision of these cysts, but to be prepared, in difficult cases, to leave any remnant of the cyst in free communication with the peritoneal cavity.

Summary

(1) Two cases are described in which, following pelvic lymphadenectomy for uterine cancer, an extra-peritoneal cyst had arisen apparently from lymphatic elements in the dissected area.

(2) The condition conforms to that already described under the name of lymphocyst. Its incidence, nature and management are briefly discussed.

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HAEMATOLOGICAL VALUES IN PREGNANT WOMEN AT TERM AND AFTER DELIVERY IN THE THREE MAIN RACIAL GROUPS IN CAPE TOWN

BY

PHILIP LANZKOWSKY, M.B., Ch.B., M.D.(Cape Town), D.C.H.(Eng.)*
Department of Child Health, University of Cape Town and
Red Cross War Memorial Children's Hospital, Rondebosch, Cape Town, South Africa

IN South Africa hitherto there has been no survey of mean haematological values (haemoglobin, packed cell volume and mean corpuscular haemoglobin concentration) in healthy White, Cape Coloured and African† women during pregnancy. The three available reports in this country (Linder and Massey, 1939; Durham, 1944; Walker, 1955) record no more than the mean haemoglobin values and only Linder and Massey consider this value in the three racial groups. The object of the present investigation was to ascertain the mean haematological values at term and after delivery in White, Cape Coloured and African women in Cape Town. This study was one of a series undertaken during an enquiry into the reasons for the local prevalence of iron-deficiency anaemia in infancy and childhood (Lanzkowsky and McKenzie, 1959; Lanzkowsky, 1959, 1960a, b). Because of the paucity of data in South Africa on mean haematological values in pregnant women an investigation into these values was thought worthy of attention.

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† The Cape Coloured people are of mixed ethnic origin and descended from various indigenous and imported groups: Slaves, Hottentots, Bushmen, Bantu and Europeans. The Africans, who are also referred to as "Bantu" or "Natives", consist of various tribes of indigenous groups of Southern Bantu. The Cape Coloured and African people are ethnically "non-White". Their social conditions are similar to those of technically less-advanced communities and they have a poor socio-economic status very much inferior to that of the White people.

Normal haematological values for pregnant women can only be assessed against a background of the physiological variations in blood volume during pregnancy and the modifications which necessarily follow.

BLOOD VOLUME ESTIMATIONS IN PREGNANCY

Willcocks (1881) was the first to suggest that the decline in red cell count and haemoglobin level in normal pregnancy might be due to physiological hydraemia. Observations on blood volume have since proved that this hydraemia does occur.

Table I presents a summary of the pertinent details of the more important reports on this subject.

The individual observations, from which the average figures of various observers are calculated, range from no increase at all in an appreciable number of cases to a maximum increase of 65 per cent above normal. The conclusion regarding the blood volume is that there is an average tendency to increase during pregnancy, the increase found by most workers amounting to approximately 25 per cent and by more recent workers up to 45 per cent over normal. The volume tends to diminish about a month before term and returns to normal levels shortly after delivery.

These latter observations must be appreciated in considering the blood-diluting effects of pregnancy, and borne in mind when considering what is normal and what is an anaemic blood

TABLE I

Summary of Literature on Blood Volume Estimations During and After Pregnancy

Author	Date	Volume Estimated	Mean Ante-partum	Mean at Term	Post-partum	Remarks and Method
Keith *et al.*	1915	Blood	+800 ml.	6,176 ml.	5,076 ml.	300 ml. blood loss. Vital Red Dye
Dieckmann and Wegner	1934a	Blood Plasma	+16% +18% } 1–13 weeks	+23% +25%	−16% −16%	Congo Red
Richter *et al.*	1934	Blood	5,988 ml. 6,117 ml.		4,117 ml. 4,308 ml.	Untreated } Brilliant Vital Treated } Red Dye
Feldman *et al.*	1936	Water				Maximum 220 days. Hb. and P.C.V. decline not parallel
Oberst and Plass ..	1936	Water				Hb. and P.C.V. decline parallel
Burwell	1936	Blood				Average tendency to increase
Burwell *et al.*	1938	Blood				Average tendency to increase
Thomson *et al.*	1938	Blood Plasma	5,117 ml. 3,710 ml. = +65%	+50%	3,964 ml. 2,106 ml.	3,920 ml. } Normal non- 2,370 ml. } pregnant. Evan's blue
Roscoe and Donaldson	1946b	Blood	2,700 ml./sq.m. (12·4 weeks) 2,975 ml./sq.m. (24·2 weeks) 3,180 ml./sq.m. (35·6 weeks)			Evan's blue
Caton *et al.*	1951	Blood R.B.C.	1,800 ml. = +45% 495 ml. = +40%			Radioactive Fe^{55} labelled R.B.C.'s
Berlin *et al.*	1953	Blood	Rapid increase (2–9 months)	+1,400 ml.	−1,100 ml.	Radioactive P_{32} labelled R.B.C.'s

picture. For this reason, many competent observers agree that it is unwise to try to interpret the significance of haemoglobin readings in pregnancy without collateral evidence from some other blood examination (Boycott, 1936; Fullerton, 1936b; Elliott, 1944).

In the present survey, packed cell volumes were estimated in addition to haemoglobin level determinations so that the mean corpuscular haemoglobin concentration could be calculated. In the absence of true anaemia the mean corpuscular haemoglobin concentration should not be affected by change in blood volume.

HAEMOGLOBIN LEVELS DURING PREGNANCY

The majority of reported investigations concerning the behaviour of haemoglobin values during pregnancy are based upon calculations of averages for large numbers of cases. For the sake of brevity most of the reports have been summarized in Table II but some are of special importance and merit short discussion.

The Medical Research Council Committee on Haemoglobin Surveys (1945), using the Haldane-Gowers method of haemoglobinometry, found a mean haemoglobin level of 11·7 g. per cent (84·6 per cent Haldane scale) in all pregnant women studied, irrespective of age, parity and stage of pregnancy. The report confirmed previous observations that there is a decline of haemoglobin value as pregnancy advances. In the first trimester in 105 pregnancies the mean haemoglobin level was 12·3 g. per cent (89·12 per cent). In the second trimester the mean value was 11·9 g. per cent (86·26 per cent) in 209 pregnancies, and in the last trimester it was 11·4 g. per cent (82·38 per cent) in 376 women. The Committee found no consistent change of mean haemoglobin level relative to parity except that rather low values were found in second pregnancies.

Linder and Massey (1939), in a Cape Town antenatal clinic, studied an unselected group of 213 healthy European and Cape Coloured women at 26 to 32, 33 to 36 and 37 to 40 weeks pregnant. They found mean haemoglobin levels of 11·74, 12·18, 12·35 g. per cent respectively in the European women and 12·26, 11·88 and 12·06 g. per cent in the Cape Coloured women. The mean haemoglobin level for 22 "natives" was 11·64 g. per cent. They found no variation in mean haemoglobin levels during the last three months of pregnancy and no significant difference between Cape Coloured and European women, whereas the haemoglobin level for the "natives" was significantly lower.

Durham (1944), examining 50 healthy Bantu females aged from 14 to 41 years attending the Alexandra township health centre in the Witwatersrand area, found a mean haemoglobin level of 12·4 g. per cent at 26 to 32 weeks, 12·5 g. per cent at 33 to 36 weeks, and 12·9 g. per cent at 37 to 40 weeks of pregnancy. He

TABLE II

Summary of Literature on Mean Haemoglobin Levels at Various Stages of Pregnancy

Author and Year		Method	Number and Subjects	Stage of Pregnancy (Weeks)	Mean Hb. (g.%)	% Subjects Below 9·7 g.% (70%)	% Subjects Below 11·0 g.% (80%)	Country
Gram	(1920)		58	1–13	(71·0)			
				14–26	(72·0)			Denmark
				27–40	(79·0)			
Kerwin and Collins	(1926)		204 A.N.C.	1–13	(83·0)			
				14–26	(83·0)			U.S.A.
				27–40	(82·0)			
Jerlov	(1927)	Autenrieth	1,143			24		Denmark
Lyon	(1929)	Sahli	177 P. and M.	40	10·4 (75·3)			U.S.A.
Galloway	(1929)	Sahli	382; 48% P.	1–13	12·6 (73)			
				14–26	11·9 (69)	65		U.S.A.
				27–40	11·4 (66)			
Harvey	(1931)	Sahli	100	Labour	13·7			U.S.A.
Esch	(1932)	Sahli	500 P., 200 M.		7·7–15·0	3	20	Germany
Davies and Shelley	(1934)	Haldane	50 A.N.C.			12		England
Dieckmann and Wegner	(1934b)	Palmer CO.	A.N.C.	10–15	13·6			
				26–35	12·5			U.S.A.
				36–40	13·0			
Davidson *et al.*	(1935)	Haldane	819 Poor Class		10·8	17·5	49·5	Scotland
Mackay	(1935)	Haldane	109 Unmarried	1–40	11·5	4·6		England
Boycott	(1936)	Haldane	222 Hospital class	1–40		11·0	22	England
Fullerton	(1936b)	Haldane	1,166 A.N.C.	12th	11·5 (83)			
				37th	10·2 (74)			Scotland
				39th	10·6 (77)			
Goodall and Gottlieb	(1936)			1–13	11·0 (80)			
Gottlieb and Strean	(1939)		200	14–26	10·4 (75)			Canada
				27–40	9·0 (65)			
Linder and Massey	(1939)	Hellige Colorimeter	213 A.N.C. European	1–40	12·48			
				26–32	11·74			
				33–36	12·18			
				37–40	12·35			South Africa
			Cape Coloured	1–40	12·32			
				26–32	12·26			
				33–36	11·88			
				37–40	12·06			
Widdowson	(1939)		100 Hospital	Early	12·8 (93)			England
				Late	10·8 (78)			
Kay and Alston	(1941)	Haldane	2,005 A.N.C. (1937)	Early	11·7 (84·7)	5·3		England
			814 A.N.C. (1941)	Early	9·8 (70·8)	39·0		
Davidson *et al.*	(1942)	Haldane	64 A.N.C.	14–26	10·6 (77)			Scotland
Hamilton and Wright	(1942)	Haldane	196 Working Class	12–20	11·0 (79)	9·2		England
			Mainly P.	40	9·7 (70)	40·3		
Sinclair	(1942)		108 A.N.C	36–40	11·7 (85)	10·0	31·0	England
Davidson *et al.*	(1943)		570 A.N.C.		10·5 (75·8)	24·0	72·3	Scotland
Meyer-Wedell	(1943)	Haldane	94 A.N.C.	1–40	10·4 (72·2)	16·0		England
Durham	(1944)	Haldane	50 A.N.C. Bantu	26–32	12·4			
				33–36	12·5	12·0	26·0	South Africa
				37–40	12·9			
Davidson *et al.*	(1944)	Haldane	61 P. A.N.C.	14–26	12·0 (86·8)			Scotland
Fullerton *et al.*	(1944)		301 A.N.C.		11·4 (82·6)	3·9		Scotland
Medical Research Council	(1945)	Haldane-Gower	690 A.N.C.	1–40	11·7 (84·6)			
			105	1–13	12·3 (89·1)	1·0		England
			209	14–26	11·9 (86·3)	5·8		
			376	27–40	11·4 (82·4)	8·8		
Roscoe and Donaldson	(1946a)	Haldane	1942 Survey:					
			50 A.N.C.	7–13	11·0 (79·8)			
			115 A.N.C.	14–26	10·4 (75·6)			
			114 A.N.C.	27–40	10·0 (72·5)			
			1944 Survey:					Scotland
			66 A.N.C.	7–13	12·1 (87·8)			
			110 A.N.C.	14–26	11·7 (85·0)			
			92 A.N.C.	27–36	10·8 (78·2)			
			43 A.N.C.	37–40	10·8 (78·0)			
Roscoe and Donaldson	(1946b)	Haldane	20	12·4	12·0			
				24·2	11·5			Scotland
				35·6	11·3			
Young *et al.*	(1946)	Alkaline Haematin	261 A.N.C.	"Early" 0–24	12·3 (82·8)		17·6	
			219 A.N.C.	"Late" 32–40	11·6 (78·6)		28·8	England
Sadovsky *et al.*	(1948)			<26	12·44	2·54		Israel
				27–40	12·22	2·56		
Walker	(1955)		43 Bantu	1–20	13·9			South Africa
			49 Bantu	21–40	13·7			
Edgar and Rice	(1956)		4,635 A.N.C.	13–16	12·9 (88·9)	2·4		
				25–28	11·8 (81·3)	11·6		England
				33–36	11·1 (76·7)	24·2		
				37–40	11·8 (81·3)	4·7		

A.N.C. = Antenatal Clinic. P. = Primiparae. M. = Multiparae.

The numbers in brackets indicate the haemoglobin level expressed as a percentage of the different standards employed by the various authors. For the sake of comparison many of these percentage values have been converted, where possible, into grammes of haemoglobin per 100 ml. of blood (g. per cent).

included primiparae and multiparae and, unlike Linder and Massey, found a definite increase in the haemoglobin level from 26 to 40 weeks.

Of special interest in South Africa is the work of Walker (1955) who showed that the mean haemoglobin level in 43 Bantu pregnant women in the Transvaal was 13·9 g. per cent in the first half of pregnancy, and 13·7 g. per cent during the second half of pregnancy in 49 pregnant women. When this is corrected for altitude (Fritzgerald's law) the levels are 12·5 g. per cent and 12·3 g. per cent respectively.

Gerritsen and Walker (1954) in the Transvaal, South Africa, showed that the Bantu take a habitually high iron-content diet. They based their views on the following observations:

(*a*) The iron intake is unusually high, sometimes as much as 200 mg. per day derived not only from the element present in their customary diet, but also as adventitious iron from iron utensils used in food preparation.

(*b*) Occasional elevated serum-iron values are found in Bantu adults.

(*c*) Hypochromic anaemia is rare in the Bantu.

(*d*) An abnormal deposition of iron is often found in tissues of adult Bantu examined at necropsy.

This high iron intake in the Bantu acts as a fortuitous iron prophylaxis during pregnancy and maintains normal values throughout pregnancy in contrast to the fall observed in White women as pregnancy progresses.

It is difficult to correlate the different findings in the various investigations of pregnancy haemoglobin values mentioned in Table II. *Inter alia*, different methods of haemoglobin estimation have been employed, determinations made at different stages of pregnancy have been combined into average results for the whole of pregnancy, and many workers have expressed results as percentages without stating the standard used by them. Nevertheless, it seems permissible to draw several general conclusions from the published data.

A fall in haemoglobin level usually occurs during pregnancy, except in the Bantu who have a habitually high dietary iron intake. This decrease in haemoglobin level during pregnancy becomes apparent at some time during the first trimester and is progressive thereafter. The lowest values are reached between 7 and 8½ months. Probably the latter has been the most frequently recorded time for the lowest values. Thereafter the haemoglobin level rises rapidly so that the values of the first trimester may be regained by the time of delivery, although usually they are not reached until the tenth day of the puerperium or even later. The average total fall in haemoglobin concentration probably does not exceed 1 gramme per 100 ml. during normal pregnancy. The degree of fall and recovery of haemoglobin values during pregnancy may differ slightly in primiparae and in multiparae. According to Roscoe and Donaldson (1946a) in multiparae it is greater at first and less pronounced in the later months. When their age was considered, however, it was found that the greater fall in multiparae was due to their greater age.

During normal labour there does not seem to be any significant variation in haemoglobin values although a transitory decrease has been noted (Bland *et al.*, 1930). There is no evidence to indicate that lactation has any effect on the haemoglobin level.

In the literature most authors have assessed the general incidence of "anaemia" in pregnancy on the haemoglobin level. But, as has been indicated, it is difficult to decide on an acceptable minimum normal value for haemoglobin which will allow for physiological variations.

Table III presents a summary of reports in which authors have recorded their findings of the incidence of patients whose haemoglobin levels were below the stated values.

All this information has been assembled from widely different sources. These series varied in several aspects of which geography, method of haemoglobinometry, age and type of subject (socio-economic status, parity, duration of pregnancy) were some of the variable factors. This makes comparison well-nigh impossible. It does reveal that approximately 13 per cent of the pregnant women had haemoglobin levels below 10 g. per cent.

Owing to the factor of blood volume changes, the degree of which varies from case to case and at different stages of pregnancy in the same case,

TABLE III

Summary of Literature Showing Percentage Incidence of Pregnant Women with Haemoglobin Values Below Certain Specified Levels

Author	Year	% Patients Who Were Below Hb. Level of (g. %)		Number of Cases in Each Series
Jerlov	1927	24·0	10·5 (76)	1,143
Galloway	1929	65·0	11·2	3,382
Lyon	1929	32·2	12·0 (70)	177
Bland *et al.*	1930	82·0	10·4 (75)	200 (Ward)
		62·0	10·4 (75)	100 (Private)
Adamson and Smith	1932	20·0	10·3 (60)	116
Schultz	1933	3·0	10·2 (74)	567
Richter *et al.*	1934	78·0	10·4 (70)	99
Balfour and Drury	1935	14·5	11·0 (80)	311
Davidson *et al.*	1935	17·5	9·7 (70)	819
		49·5	11·0 (80)	
Mackay	1935	56·0	11·6 (84)	109
McGeorge	1935	16·0	10·4 (75)	100
Bethell	1936	70·0	11·3 (70)	66
Boycott	1936	22·0	11·2 (80)	222
		11·0	9·8 (70)	
Fullerton	1936a	49·5	11·0 (80)	819
		17·5	9·3 (70)	
Reid and Mackintosh	1937	10·2	9·7 (70)	1,100
		54·1	11·7 (85)	
Kay and Alston	1941	5·3	9·7 (70)	2,005
Hamilton and Wright	1942	16·8	9·7 (70)	392
Sinclair	1942	5·9	9·7 (70)	
		27·7	11·0 (80)	
Davidson *et al.*	1943	24·0	9·7 (70)	570
		72·3	11·0 (80)	
Meyer-Wedell	1943	16·0	9·7 (70)	392
Durham	1944	26·0	11·2	50 Bantu
		12·0	9·8	
Fullerton *et al.*	1944	3·9	9·7 (70)	301
Medical Research Council	1945	1·0	9·7 (70)	1–13 weeks
		5·8	9·7 (70)	14–26 weeks
		8·8	9·7 (70)	27–40 weeks
Dieckmann	1945	63·0	12·0	
		12·0	10·0	
Sadovsky *et al.*	1948	2·54	9·7 (70)	1–26 weeks
		2·56	9·7 (70)	27–40 weeks
Scott and Govan	1949	20·1	10·4 (65)	4,595
Lund	1951	25·0	10·0	4,015
Benstead and Theobald	1952	6·6	10·0	2,000
		12·1	10·5	<16 weeks pregnant
		18·9	11·0	
		60·0	12·0	
Doyle and McGrath	1954	31·4	10·0	1,000
Gatenby and Lillie	1955	23·8	10·0	4,314
		9·0	9·0	
Gatenby	1956	24·0	10·0	5,000 in 1953
		12·0	10·0	5,000 in 1954
		11·0	10·0	5,000 in 1955
Kerr and Davidson	1958	13·7	10·4	225
		78·1	12·6	<23 weeks pregnant

The numbers in brackets indicate the haemoglobin level expressed as a percentage of the different standards employed by the various authors. For the sake of comparison, many of these percentage values have been converted into grammes of haemoglobin per 100 ml. of blood (g. per cent).

it is not possible to lay down a standard of haemoglobin level as a normal which will be applicable for all pregnant women. Dieckmann and Wegner (1934b) gave 10·04 g. per cent (72 per cent Haldane; 58 per cent Sahli) as the lowest acceptable normal value, whereas Adair *et al.* (1936) in a large-scale statistical survey decided on a figure of 10·16 g. per cent. Boycott (1936) was less dogmatic and regarded 9·7 g. per cent (70 per cent Haldane) as a usual normal lower limit, but considered that figures even lower could sometimes be normal. Bethell (1936) calculated, on a basis of 25 per cent increase in blood volume, that the maximum decrease in haemoglobin value that could be attributed solely to hydraemia was to a level of 11·3 g. per cent. Labate (1940) considered 11·0 g. per cent (80 per cent Haldane) to be the lowest limit of normal.

Packed Cell Volume Values During Pregnancy

During pregnancy there is a reduction in the packed cell volume value. Table IV summarizes the reported findings of various workers.

The conclusion from these observations is that the mean packed cell volume is reduced during pregnancy to an average of 35 per cent with a lowest recorded value of 31·5 per cent. Any figure below this must be regarded as being less than the acceptable normal and indicative of anaemia.

Mean Corpuscular Haemoglobin Concentration Values During Pregnancy

The mean corpuscular haemoglobin concentration gives direct evidence of the presence or absence of iron-deficiency anaemia (Discombe, 1954; Wintrobe, 1956; *South African Medical Journal*, 1959). Most normal subjects have mean corpuscular haemoglobin concentration values between 32 and 35 per cent, although values between 30 and 32 per cent may occur in normal subjects but are suggestive of mild iron-deficiency anaemia (Discombe, 1954). Patients with marked iron-deficiency anaemia have values below 30 per cent. Simpson (1954) showed in a series of 216 pregnant women that the mean corpuscular haemoglobin concentration varies little through pregnancy and that it is the only reliable and true index of iron-deficiency anaemia. He gave the critical lower level as 30·7 per cent. Discombe (1954) stated that a mean corpuscular haemoglobin concentration level of 30·2 per cent at full term indicated iron deficiency but not necessarily anaemia.

Present Investigation

Material

A total of 243 women were examined at term (during the first stage of labour). Of these 201 were examined at 3 months after delivery. In the series there were 131 Whites, 77 Cape Coloureds and 35 Africans. They were a random selection of women attending antenatal clinics and confined at various maternity institutions attached

TABLE IV

Summary of the Literature on Mean Packed Cell Volume Values at Various Stages of Pregnancy and in Post-partum Period

Authors	Date	Trimesters			At Term	Post-partum
		1st	2nd	3rd		
Plass and Bogert	1924	35·6	31·5	—	—	34·7
Skajaa	1929	—	—	—	36·4	43·0
Dieckmann and Wegner	1934b	39·6	—	36·9	38·3	37·7
Adair *et al.*	1936		35 to 44		—	—
Thomson *et al.*	1938	—	38·0	32·0	—	38·0
Labate	1940	—	38·9	—	—	—
Simpson	1954	—	39·0	35·1	—	—

TABLE V

Distribution of Ages of 243 White, Cape Coloured and African Pregnant Women

Race	Number of Cases	Age in Years				Mean Age	S.D.
		Below 20	20–30	31–40	Over 40		
White	131	10	88	30	3	26·11	5·78
Cape Coloured ..	77	7	48	15	7	26·76	6·71
African	35	6	22	5	2	24·71	7·15

to the University of Cape Town. It is likely that this sample contained an undue proportion of primigravidae and those who had previous obstetric complications because the investigation was done on patients delivered in an institution. All these women were given a routine general medical examination at their first attendance and were found to be healthy. Serological tests for syphilis were negative in all. Only those who had full-term normal pregnancies, normal labours and who delivered without incident were included. Any woman who had haemorrhagic episodes before, during or after delivery was excluded, as were cases of mid-forceps, rotation and breech deliveries or any deliveries requiring anaesthetics. None had received prophylactic iron therapy during pregnancy.

The ages ranged from 17 to 41 years in the White women, 18 to 43 years in the Cape Coloured and 16 to 42 years in the Africans, with mean ages of 26·11, 26·76 and 24·71 years in the respective racial groups. This is shown in Table V.

The parity ranged from 1 to 10, 1 to 19 and 1 to 7 with a mean of 2·38, 3·08 and 2·44 in the groups of White, Cape Coloured and African women respectively. Fifty-three of the White, 37 of the Cape Coloured and 16 of the African women, that is, somewhat less than half of each group, were primiparae. This is shown in Table VI.

The mean income per week of the families from which these women came was £14·09, £5·27 and £3·68 for White, Cape Coloured and African women respectively. According to the criteria adopted by Bronte-Stewart *et al.* (1955) and Moodie (1959) these amounts place them in the "medium income" groups in their respective sections of the community.

Methods

Blood investigations were done on venous blood from the anterior cubital vein. The haemoglobin estimations were done by the oxyhaemoglobin method using the Klett-Summerson colorimeter previously calibrated for the purpose against standard haemin and cyanmethaemoglobin solutions. Packed cell volume estimations were made by the standard Wintrobe procedure (Wintrobe, 1929).

TABLE VI

Distribution of Parity of 243 White, Cape Coloured and African Pregnant Women

Race	Number of Cases	Parity			Mean Parity	S.D.
		1st	2nd	3rd or More		
White	131	53	36	42	2·38	1·74
Cape Coloured ..	77	37	12	28	3·08	3·33
African	35	16	8	11	2·44	1·99

TABLE VII

Mean Haemoglobin Values and Incidence of Haemoglobin Ranges in Healthy White, Cape Coloured and African Pregnant Women at Term

Race	No. of Cases	Haemoglobin Range g. %											Mean g. %	S.D.
		6·0–6·9	7·0–7·9	8·0–8·9	9·0–9·9	10·0–10·9	11·0–11·9	12·0–12·9	13·0–13·9	14·0–14·9	15·0–15·9	16·0–16·9		
White ..	131			3·1 (4)	8·4 (11)	25·2 (33)	26·7 (35)	21·4 (28)	12·2 (16)	0·8 (1)	1·5 (2)	0·8 (1)	11·54	1·40
Cape Coloured	77	2·6 (2)	2·6 (2)	6·5 (5)	7·8 (6)	22·1 (17)	33·8 (26)	19·5 (15)	2·6 (2)	1·3 (1)	1·3 (1)		11·00	1·58
African ..	35				11·4 (4)	17·1 (6)	31·4 (11)	22·9 (8)	17·1 (6)				11·62	1·24

To facilitate comparison the number of individuals in each haemoglobin range is expressed as a percentage of the number in each racial group. The numbers in brackets indicate the actual number of cases in each haemoglobin range.

TABLE VIII

Mean Packed Cell Volume Values and Incidence of Packed Cell Volume Ranges in White, Cape Coloured and African Pregnant Women at Term

Race	Number of Cases	Packed Cell Volume Range %					Mean %	S.D.
		30–35	36–40	41–45	46–50	51–55		
White	130	13·1 (17)	44·6 (58)	33·1 (43)	8·5 (11)	0·8 (1)	39·89	4·19
Cape Coloured ..	70	20·0 (14)	47·1 (33)	28·6 (20)	2·9 (2)	1·4 (1)	38·87	4·59
African	33	6·1 (2)	36·4 (12)	42·4 (14)	12·1 (4)	3·0 (1)	41·21	4·22

To facilitate comparison the number of individuals in each P.C.V. range is expressed as a percentage of the number in each racial group. The numbers in brackets indicate the actual number of cases in each P.C.V. range.

TABLE IX

Average Mean Corpuscular Haemoglobin Concentration Values and Incidence of Mean Corpuscular Haemoglobin Concentration Ranges in White, Cape Coloured and African Pregnant Women at Term

Race	No of Cases	Mean Corpuscular Haemoglobin Concentration Range %							Mean %	S.D
		20·0–22·5	22·6–25·0	25·1–27·5	27·6–30·0	30·1–32·5	32·6–35·0	35·1–37·5	37·6–40·0		
White	130	0·8 (1)	2·3 (3)	16·2 (21)	56·9 (74)	21·5 (28)	1·5 (2)		0·8 (1)	28·87	1·83
Cape Coloured	70		4·3 (3)	21·4 (15)	55·7 (39)	14·3 (10)	2·8 (2)		1·4 (1)	28·35	4·21
African ..	33		3·0 (1)	33·3 (11)	57·6 (19)	6·1 (2)				28·10	1·65

To facilitate comparison the number of individuals in each M.C.H.C. range is expressed as a percentage of the number in each racial group. The numbers in brackets indicate the actual number of cases in each M.C.H.C. range.

RESULTS

Tables VII, VIII and IX show the mean haemoglobin, packed cell volume and mean corpuscular haemoglobin concentration values respectively and the incidence of these haematological ranges in 243 pregnant women at term in the three racial groups. The mean haemoglobin levels were 11·54 g. per cent, 11·00 g. per cent and 11·62 g. per cent for White, Cape Coloured and African pregnant women respectively. The mean packed cell volume values were 39·89 per cent, 38·87 per cent and 41·21 per cent and the average mean corpuscular haemoglobin concentration levels were 28·87 per cent, 28·35 per cent and 28·10 per cent for the three respective racial groups of pregnant women at term.

Table X shows the mean haemoglobin values and the incidence of haemoglobin ranges in 201 of these women 3 months after delivery. The mean levels were found to be 12·47 g. per cent for White, 11·25 g. per cent for Cape Coloured and 12·09 g. per cent for African women.

TABLE X

Mean Haemoglobin Values and Incidence of Haemoglobin Ranges in Healthy White, Cape Coloured and African Women at 3 Months Post-partum

Race	No. of Cases	Haemoglobin Range g. %										Mean g. %	S.D.
		6·0–6·9	7·0–7·9	8·0–8·9	9·0–9·9	10·0–10·9	11·0–11·9	12·0–12·9	13·0–13·9	14·0–14·9	15·0–15·9		
White ..	112				1·8 (2)	3·6 (4)	23·2 (26)	39·3 (44)	26·8 (30)	3·6 (4)	1·8 (2)	12·47	1·04
Cape Coloured	63	3·2 (2)		1·6 (1)	1·6 (1)	11·1 (7)	41·3 (26)	31·7 (20)	7·9 (5)	1·6 (1)		11·25	2·43
African ..	26				3·9 (1)	11·5 (3)	23·0 (6)	42·3 (11)	19·2 (5)			12·09	1·05

To facilitate comparison the number of individuals in each haemoglobin range is expressed as a percentage of the number in each racial group. The numbers in brackets indicate the actual number of cases in each haemoglobin range.

DISCUSSION

The present findings could only be compared with those series in which the authors have specified that the blood examinations were done at corresponding times of pregnancy.

The mean haemoglobin levels in these three racial groups are higher than the mean haemoglobin levels at term established by many workers. Gottlieb and Strean (1939); Hamilton and Wright (1942) and Roscoe and Donaldson (1946a, b) all give mean haemoglobin levels at term lower than those found in the present investigation. Galloway (1929), Sinclair (1942), Medical Research Council (1945) and Young *et al.* (1946) give levels almost identical with the present findings. The haemoglobin levels of Dieckmann and Wegner (1934b), Linder and Massey (1939), Durham (1944) and Sadovsky *et al.* (1948) are slightly higher.

The proportion of pregnant women with haemoglobin levels below 10 g. per cent in the present series was 11·5 per cent for White, 19·5 per cent for Cape Coloured and 11·4 per cent for African pregnant women at term. This compares with the figure of 13 per cent calculated from a survey of the literature quoted in Table III. If an arbitrary level of 10 g. per cent is taken as the lowest level of normal haemoglobin value, then on this criterion alone, it appears from the above findings that iron-deficiency anaemia is not unduly prevalent in pregnant women in Cape Town.

The mean packed cell volume values in the three racial groups were between 38·87 per cent and 41·21 per cent which are values well above the usual normal level for pregnancy. These results support the conclusion from haemoglobin estimations that iron-deficiency anaemia is not unduly prevalent in these pregnant women at term. The mean packed cell volume values in the White and Cape Coloured races were slightly higher, and in the African considerably higher, than the values given by Dieckmann and Wegner (1934b). The differences are even greater when the present figures are compared with those of Thomson *et al.* (1938).

The average mean corpuscular haemoglobin concentration levels in the three racial groups were between 28·10 and 28·87 per cent. The mean corpuscular haemoglobin concentration is generally acknowledged to be the most revealing index of iron-deficiency anaemia. The lowest level acceptable as normal appears to be 30 per cent. Taking this value as the critical level, 76·2 per cent of White, 81·4 per cent of Cape Coloured and 93·9 per cent of African women in this series were anaemic. This could not be due merely to blood dilution, since the packed cell volume values were almost normal.

Accepting the mean corpuscular haemoglobin concentration level as the most reliable index of iron-deficiency anaemia available for routine use, one must conclude that the incidence of iron-deficiency anaemia in all three racial groups of pregnant women is high. This contrasts with the deduction made from consideration of the mean haemoglobin and packed cell volume levels. The incidence of iron-deficiency anaemia is far higher than found by the studies of haemoglobin level which, on the basis of 10 g. per cent as a minimum normal, indicated the incidence to be less than 20 per cent.

This high incidence of maternal iron-deficiency anaemia is not surprising, since the physiological iron requirements during pregnancy are considerable and the dietary iron intake is probably

insufficient in most cases. Neuweiler (1938) estimated that the total foetal requirement of iron is 375 mg. Several workers have calculated the daily dietary iron requirement of pregnant women. Coons (1932) estimated this to be 14·7 mg., Davidson *et al.* (1935) suggested 15 mg. and Ohlson and Daum (1935), Ebbs *et al.* (1941) and the National Research Council (U.S.A.) (1947) have agreed with this figure, whereas McCance and Widdowson (1946) give 16 to 20 mg. as the minimum daily iron requirement during pregnancy. This amount of iron need may be met by the diets of the medium-income Whites but it is unlikely to be provided by the diets of the non-White racial groups in Cape Town.

At three months post-partum it was found that the mean haemoglobin levels had risen above the term values in all three racial groups of women. The rise was greatest in the White and least in the Cape Coloured women. The better recovery in the White women may also indicate better dietary iron intake in this racial group.

Cessation of the foetal demand should permit improvement. The fact that improvement occurred indicates that these women had a normally functioning haematopoietic system. The relatively poor rise in haemoglobin in the post-partum period suggests that there was inadequate reserve of the materials needed for the rapid restoration of a normal blood picture. The store must have been exhausted by the demands of pregnancy and none of the mothers in this series received any medicinal iron either before or after delivery.

Subsequent work has revealed that the administration of iron during pregnancy in a comparable control group of Cape Coloured pregnant women has resulted in a significant rise in haemoglobin, packed cell volume and mean corpuscular haemoglobin concentration values at term. At 3 months post-partum the mean haemoglobin level in this treated group was statistically significantly higher than in the untreated group of women (Lanzkowsky, 1961). This response to iron therapy confirms the finding that iron-deficiency anaemia is commonly present during pregnancy and in the post-partum period in women in Cape Town.

Summary

(1) A review is given of the literature on blood volume estimations, haemoglobin levels, packed cell volume and mean corpuscular haemoglobin concentration values during pregnancy. The physiological variations of blood volume in pregnancy influence the haemoglobin level. It is indicated that the only true index of iron-deficiency anaemia available for routine use is the mean corpuscular haemoglobin concentration level, and a value of approximately 30 per cent is quoted as the critical lower level.

(2) Haematological values were determined in 243 healthy women attending antenatal clinics in Cape Town. Of these, 131 were Whites, 77 Cape Coloureds and 35 Africans.

(3) The mean haemoglobin levels were 11·54, 11·00 and 11·62 g. per cent; the mean packed cell volume levels were 39·89, 38·87 and 41·21 per cent; and the average mean corpuscular haemoglobin concentration levels were 28·87, 28·35 and 28·10 per cent for White, Cape Coloured and African pregnant women at term respectively.

(4) At 3 months post-partum the mean haemoglobin levels in 201 of these women were found to be 12·47, 11·25 and 12·09 g. per cent for White, Cape Coloured and African women respectively.

(5) Taking 30 per cent as the lowest mean corpuscular haemoglobin concentration level acceptable as normal, 76·2 per cent of White, 81·4 per cent of Cape Coloured and 93·9 per cent of African women in this series were anaemic. This high incidence of iron-deficiency anaemia in healthy pregnant women in Cape Town is ascribed to the inadequacy of the diets in this community to meet the physiological demands of pregnancy on iron nutrition.

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APLASTIC ANAEMIA IN PREGNANCY

BY

DAVID C. FIGGE, M.D.

DENNIS M. DONOHUE, M.D.

AND

RUSSELL R. DE ALVAREZ, M.D.

From the Department of Obstetrics and Gynecology and the Division of Hematology, University of Washington, School of Medicine, Seattle 5, Washington, U.S.A.

IRON deficiency anaemia, megaloblastic anaemia, and hypoplastic anaemia comprise the three common types of true anaemia described as occurring in pregnancy. Even though the co-existence of the anaemia and the pregnancy is frequent, no cause and effect relationship has ever been definitely proved. Any specific anaemia may complicate or be complicated by pregnancy. Again, the effect of the pregnancy in all instances is poorly defined. One of the most serious of this group of anaemias is primary refractory or aplastic anaemia.

Although the term "aplastic anaemia" has gained wide acceptance in clinical medicine, it is not precise nor is it really descriptive of any specific feature since anaemia is only one phase of the generalized depression of formed blood elements. The designation is usually applied to cases of severe refractory pancytopenia where gross evidence of increased blood destruction is absent and infiltrative disease of the marrow cannot be demonstrated. The characteristic haematological findings are anaemia, leukopenia and thrombocytopenia. Definite evidence of decreased marrow production of all formed elements of the blood is necessary to support the diagnosis, although this is not invariably confirmed by marrow examination, even in cases with specific aetiology. Such bone marrow depression may be the result of exogenous or endogenous toxic origin. The mechanisms involved in the marrow depression are speculative. The aetiology insofar as a specific causal agent is often obscure and, where such agents are suspect, the aetiological relationship is difficult to establish.

Aplastic anaemia is a rare complication of pregnancy. It is noteworthy that the first reported case of aplastic anaemia, described by Ehrlich in 1882, occurred in a young pregnant woman (1888). Although he did not apply any name to the condition he described, he did conclude that the underlying pathology was depression of bone marrow function. Only scattered subsequent reports of cases of pregnancy complicated by aplastic anaemia have appeared in the literature. In 1942 Hurwitt and Field presented a case which terminated fatally. They concluded from the review that pregnancy might play an "etiologic or conditioning" role in the occurrence of this condition in pregnancy and felt that immediate interruption of pregnancy was mandatory.

More recently, Lachman, Lund and Vinther-Paulsen (1954) after a search of the world literature were able to collect twelve cases in which they felt that the diagnosis of aplastic anaemia associated with pregnancy was either "most probable or certain" and to which they added one of their own. Review of the limited data presented by some of these cases leaves the diagnosis in many instances open to question.

Eleven cases were diagnosed in the ante-partum period with a maternal mortality of 45 per cent. In all of the reported instances either spontaneous labour occurred or labour was induced shortly after establishment of the diagnosis. In the two instances where abdominal surgery was carried out at delivery or during the puerperium (one premature Caesarean section and one hysterectomy) both patients expired of bleeding complications in the post-operative period. Five patients among those reported developed either a remission of the disease or apparent recovery. No instance has been reported where pregnancy was allowed to proceed to term with survival of the patient. As a result the general rule has been to terminate all pregnancies once the diagnosis is established.

This paucity of clinical information regarding the aplastic anaemia as a complication of pregnancy has led to conclusions and recommendations which might well be challenged. Certainly no concrete evidence has been introduced to show that pregnancy serves as a contributing cause to the development or enhancement of aplasia of the bone marrow. As Sturgis (1955) comments: "if there is a causal relationship, it is apparently rarely evoked, as this is an extremely uncommon complication of the gravid state". We have preferred to consider this condition as a coincidental complication of pregnancy, or a medical condition complicated by pregnancy, rather than consider the pregnancy as a related causal mechanism. Similarly the limited reports available do not bear out the contention that the complicating disease in this instance is significantly affected by the presence of the pregnancy. It seems more likely that the natural pattern of this process occurs irrespective of the pregnancy and that recovery or remission, if it occurs, is related to the simple passage of time.

The impetus for our review of this problem was stimulated by the following case, which is reported in some detail.

Case Report

Mrs. B.G., a 27-year-old white female, gravida-3, para-1, was first seen in consultation on 22nd July, 1958, with a history of progressive weakness, fatigue and dyspnoea. Her last normal menstrual period occurred on 14th November, 1957. The calculated date of confinement was 21st August, 1958. She had been followed in her prenatal course by physicians of a nearby Naval station dispensary. In November, 1957 she was treated for pyelitis with chloromycetin 1 gram daily for three days followed by gantrisin, 3 grams daily for seven days. Her initial haemoglobin on 26th March, 1958, was 10 grams per cent. This was repeated on 15th July, 1958, and reported as 11·2 grams per cent. On 15th July, 1958, the patient complained of weakness, fatigue and dyspnoea. She was treated with phenobarbital 15 mg. b.i.d., mersalyl with theophyllin, and acetazoleamide 500 mg. daily for seven days. Her symptoms were progressive. Repeat haematological studies carried out one week later revealed the haemoglobin to be 5 grams per cent. At this time there was no evidence of subjective or objective bleeding or haemorrhagic changes. She was afebrile and showed no evidence of jaundice.

The patient had had no serious illnesses and never required hospitalization except for pregnancy and delivery. In 1956 a spontaneous abortion at three months occurred, completed with pitocin and ergotrate. In January, 1957 she delivered a male infant weighing 7 pounds 3 ounces after an uneventful labour. The prenatal and post-partum course during this pregnancy were uneventful.

When initially examined the patient was ambulatory but fatigued, well nourished and appearing pale and chronically ill. B.P. was 120/70, pulse 100 per minute, temperature 98° and respirations 24 per minute. Her skin was extremely pale but with no evident icterus and no petechiae. The heart-beat was forceful, there was no evident cardiomegaly and the cardiac rhythm was normal sinus in type. No murmurs were heard. The liver and spleen were not palpable. The gravid uterus was felt 30 cm. above the symphysis with a foetus in breech presentation; the foetal heart tones were 140 per minute and clear and distinct.

Chest X-ray, electrocardiogram and urine analysis were normal on admission. The haematocrit was 8 per cent, the white blood count 2,000 with 34 neutrophils, 64 lymphocytes and 2 monocytes. The platelet count was 19,000 per c.mm. and no reticulocytes were seen. Sedimentation rate was 40 mm. per hour, a direct Coombs' reaction was negative, M.C.V. was 95 μ^3, M.C.H. was 55 $\mu\mu$ and M.C.H.C. 55 per cent. Bleeding time was in excess of one hour and clotting time was 8 minutes; there was no clot retraction in one hour and only partial retraction in 24 hours. Serum bilirubin was 0·42 mg. per cent, total proteins 4·98 grams per 100 c.cm., serum electrolytes were normal and serum protein electrophoretic pattern was normal for all fractions. A bone marrow aspirate was obtained with adequate material and revealed only a reticulum with absence of all foreign elements.

The patient was admitted to the hospital on 22nd July, 1958. A diagnosis was made of 36-weeks intrauterine gestation complicated by aplastic anaemia and pancytopenia. It was felt that the patient's cardiac output was probably 3–4 times normal with probable compensation for the decreased haemoglobin and red cell volume.

Following admission the patient was slowly transfused with 500 c.cm. of packed red cells over a twelve-hour period in an upright sitting position with marked subjective and objective improvement. The haematocrit 48 hours after admission had risen to 15 per cent and the patient tolerated ambulation and limited activity with ease. The symptoms of faintness and fatigue disappeared. An additional 500 c.cm. of packed red cells were given on 29th July with a response in the haematocrit to 20·5 per cent although the white blood count remained 1,100.

During the initial five weeks of hospitalization, the patient was maintained on a conservative management. During this period she received a total of twelve transfusions of 250 c.cm. of packed red blood cells (3,000 c.cm.), gradually raising the haematocrit to and maintaining it at 26–28 per cent. There was no improvement in the leucopenia or thrombocytopenia and no reticulocyte response evident during this period. Ten days after admission the patient began to exhibit episodes of bleeding from the gums and developed petechiae over the abdomen and lower thorax. She was placed on meticorten, 20 mg. orally daily at this time. On 17th August, following catheterization the patient developed gross haematuria which cleared spontaneously over the following four days.

Spontaneous onset of labour occurred on the morning of 1st September, 1958. Progress was slow with regular contractions and there was no bleeding or bloody show. At 9.00 a.m. the cervix was 6 cm. dilated, the foetus was in ORP position at –1 station. At 11.00 a.m. the membranes were artificially ruptured after no further progress. Good contractions became established with a heavy bloody show. At 2.00 p.m. the patient was taken to the delivery room after spontaneous rotation ORP to ORA with the vertex on the perineum. Delivery was accomplished under general anaesthesia by low forceps without episiotomy of a healthy male infant weighing 7 pounds. The placenta was expressed intact. A small first degree perineal laceration was sustained and closed with chromic catgut. An estimated blood-loss of 300 ml. was sustained. After prolonged observation in the delivery room she was returned to her post-partum bed in good condition.

The infant was healthy, mature and without developmental anomalies. Laboratory studies revealed no neonatal haematological defects and the neonatal course was uncomplicated.

The placenta appeared grossly normal; microscopic sections revealed no pathological changes.

Eight hours following delivery the patient was re-evaluated because of a steady and progressive fall in blood pressure to 78/50 with an associated tachycardia of 120 per minute. Eight to ten perineal pads had been moderately saturated since delivery but there was no active bleeding. The fundus was firm and abdominal and pelvic examination revealed no evidence of concealed blood loss. She was alert but pallid. No measurable urinary output had been obtained but intake had been minimal. Extensive pudendal oedema and haemorrhagic ecchymoses were present.

During the following eight hours the patient gradually improved with a return of the blood pressure and pulse to normal levels and an output of 200 ml. concentrated urine. During the first week post-partum the patient exhibited a relatively normal course. Lochia gradually diminished from 7 pads to 3–4 pads daily. There was slight haematuria but no difficulty in voiding. The perineal oedema became less pronounced and her haematocrit on 3rd September, 1958, the 2nd post-partum day, was 19 per cent. She received transfusions of 500 ml. of packed red blood cells on 6th September after a haematocrit determination of 13 per cent. On the 7th post-partum day a typical puerperal endometritis and parametritis became evident with pyrexia to 102°. Penicillin and tetracycline therapy were administered with resolution of the infection and return to the afebrile state within four days. An additional 500 ml. of red blood cells were transfused on 10th September bringing the haematocrit to 20 per cent. Fundal involution was normal and she was discharged on 15th September. She had received a total of 3,750 ml. of packed red blood cells during this admission.

The patient was re-admitted to the hospital four days later on 19th September, 1958, her 18th post-partum day, with complaints of headaches, fatigue, malaise and progressive weakness. Vaginal bleeding following discharge had increased to 6–8 pads daily despite ergotrate. Upon admission her appearance was essentially unchanged except for marked pallor. Petechiae were present over the lower abdomen. The admission haematocrit was 10 per cent, white blood count 2,000 with a normal differential. She received a transfusion of 1,000 ml. fresh whole blood shortly after admission. Pelvic examination revealed normal external genitalia with a healed perineal laceration. The mucosa was pale but intact. The cervix was dilated to 2½ cm. with a contained blood clot. The uterus was regular in outline and 8-weeks gestational size. Induration was present in the left parametrium but no haematoma was palpable.

During the next forty-eight hours the uterus repeatedly became distended with blood clots, palpable abdominally and would empty with stimulation. On the morning of 23rd September, the 22nd post-partum day, the patient had an episode of syncope and brief coma with the pulse rate reaching 150 per minute. The uterus was palpable abdominally. She received rapid transfusions of 2,000 ml. of whole fresh blood during that day raising the haematocrit to 30 per cent and the platelet count to 60,000. At this time the bleeding-time became normal at seven minutes as done by the standard Lee and White technique and clot retraction was normal by qualitative technique. Dilatation and curettage was carried out that evening productive of large blood clots and a scant amount of tissue. Brisk bleeding ensued following curettage, gradually subsiding under ergotrate stimulation and manual compression of the uterus. Pathological examination revealed the tissue to contain some very distinct small placental villi. The material was predominantly blood clot—some of which had been present long enough so that calcium deposition could be identified.

Following the procedure the pattern of bleeding temporarily subsided but a recurrence of the uterine infection became evident with febrile episodes above 102°. Antibiotic therapy was again instituted with a slow response toward normal. The patient continued to saturate 7–9 perineal pads daily. Bleeding time on 24th September was 31 minutes and the haematocrit had fallen to 19 per cent. The patient was given intravenous and oral oestrogens in large doses with no immediate effect.

After considerable deliberation it was felt that the patient should be scheduled for abdominal hysterectomy if no improvement with further conservative measures could be effected. During the next two weeks, however, a very gradual but definite decrease in the amount of vaginal bleeding became apparent and she continued on the conservative programme of observation and transfusion. On 5th October, 1958, the oestrogen therapy was discontinued and she was given norethindrone, 30 mg. daily. On 10th October, the 39th post-partum day, the vaginal bleeding had decreased to an estimated 30 ml. daily and she was discharged after transfusion with packed red cells to a 30 per cent haematocrit. A total of 1,000 ml. packed red cells and 2,000 ml. whole blood was given during this admission.

A close follow-up was maintained with the patient. The norethindrone was discontinued after 11 days therapy and she had a menstrual-like episode of bleeding requiring 4–5 pads daily for three days, 72 hours later. Three weeks following discharge, 9 weeks post-partum, the haematocrit was 23·5 per cent. No reticulocytes were present in the peripheral blood and the platelet count was 20,000. A complete repetition of all the serological studies revealed normal findings except for the anaemia and pancytopenia. Petechiae were still present over the abdomen. Pelvic examination revealed normal findings. The uterine involution was complete and the fundus was of normal size. There was no vaginal bleeding.

The patient's husband received orders for transfer to Pensacola, Florida. The patient received a transfusion of 500 ml. of packed red blood cells prior to leaving. Subsequent to transfer the patient had two relatively "normal" menstrual periods. The first occurred on 3rd December, 1958, 12 weeks following delivery, and the second on 7th February, 1959. There was no evident remission of the haematologic picture and transfusions were required approximately every two weeks.

The patient was followed at the Naval Hospital in Pensacola, Florida and managed with multiple blood transfusions and prednisone. She remained symptom-free and at normal activity until 28th March, 1959 when she was admitted with the sudden onset of abdominal pain, radiating to the right shoulder and chest. She was initially treated with antibiotics and the administration of 1,000 ml. of blood. A diagnosis of intra-abdominal haemorrhage was confirmed by culdocentesis. The patient stabilized briefly and appeared to be clinically improved, but before laparotomy could be performed she became semi-comatose with gastric and urinary bleeding. She expired on 31st March, 1959, three days after admission. Autopsy confirmed the diagnosis of aplastic bone marrow. Two thousand ml. of blood were present in the peritoneal cavity, originating from a 6 cm. ruptured right ovarian cyst. Microscopic sections of this cyst indicated it was probably a corpus luteum cyst. Haemorrhage occurring from all serous membranes was present in addition to the presence of subarachnoid and cerebral haemorrhage. Haemosiderosis of the liver and spleen was identified.

Discussion

This presentation represents a case of pregnancy complicated by bone marrow failure and resulting pancytopenia. The diagnosis rests upon the presence of a severe normocytic normochromic anaemia with leucopenia and thrombocytopenia, together with the severe bone marrow depression confirmed by biopsy. The general course of management elected with this patient was conservative. In our opinion the rationale and value of interruption of pregnancy under these circumstances has not been established. There is no valid evidence that pregnancy is in any way related to this complication of pregnancy in a causative way. There is no suggestion in the course of this patient that the pregnancy had either an ameliorating or deleterious effect upon the progress of the complicating disease or upon the final outcome; likewise there is no evidence that delivery of the pregnancy had any effect upon the natural course of the disease.

Aplastic anaemia however is a condition that might be expected to produce serious effects upon the course of the pregnancy. These effects seem to be associated primarily with platelet deficiency and anaemia. The haemorrhagic consequences are illustrated in the pattern of this patient through pregnancy, labour, delivery and the puerperium. Bleeding complications relating to the thrombocytopenia first became evident shortly after admission in the form of petechiae over the abdomen and thorax, and gum bleeding, and haematuria. The patient was placed on adrenal corticosteroids in an attempt to produce a stimulatory effect upon the bone marrow and because of reported reversal of any increased cellular destruction resulting from auto-immune mechanisms. There was no evidence of any positive response in this patient. Our primary therapeutic aim during the period

of foetal maturation was to maintain the haematocrit at a level which would prevent symptomatic hypovolaemia. This maintenance required a total of 3,000 ml. of packed red blood cells during the ante-partum period. Packed red cells were employed in transfusion since the patient's basic deficit was in formed blood elements rather than total blood loss. It was our hope during this phase of management that there would be insufficient time for the development of significant platelet antibodies and that, when needed, fresh whole blood transfusions would be used in an effort to control bleeding.

The patient was allowed to continue to term to await spontaneous onset of labour since we felt that there probably was no causative relationship between the pregnancy and the pancytopenia and that nothing was to be gained by premature interruption. The labour was completely normal and uncomplicated. Delivery was carried out under light cyclopropane anaesthesia to avoid the potential complications of bleeding that might develop at the spinal, local, or nerve block injection sites. Since the immediate control of bleeding at the placental site was accomplished by spontaneous uterine contraction and vascular constriction, immediate blood loss with delivery and in the third stage was not excessive.

Infection during the puerperium was anticipated and occurred. It was our feeling that antibiotic therapy would be best utilized when such a situation arose rather than prophylactically over a protracted period of time. Late postpartum haemorrhage proved the most difficult issue. The problem of haemorrhage and its sequelae posed a therapeutic dilemma since we were unable effectively to offset the cause. Surgical removal of the bleeding organ, in this case the uterus, is not only medically unsound, but might precipitate even worse consequences. It should be considered only as a final resort. Bleeding from the area of dissection in addition to the problems of infection, embolism, etc., might be anticipated if such a procedure were employed.

At the time of her second admission, the immediate and urgent dilatation and curettage controlled the uterine bleeding. Temporary improvement of the coagulation mechanism was achieved by the rapid transfusion of whole fresh blood; this probably was as important as the curettage. Elevation of the platelet count to 60,000 apparently was the feature that shifted the balance toward a favourable outcome. It is important to bear in mind that it is possible to transfuse platelets by the simple expedient of collecting fresh blood into plastic equipment and then transfusing it without delay.

As the patient continued to show excessive puerperal uterine bleeding, oestrogens were administered in an attempt to produce reparative proliferation of the endometrium and to hasten obliteration of the placental site of bleeding. Whether this occurred is open to question. Since continued use of oestrogen could have resulted in breakthrough bleeding and its withdrawal result in withdrawal bleeding, norethindrone was substituted. By conversion of the endometrium to a secretory state, withdrawal bleeding was obviated and, if indicated, the patient could have been maintained amenorrhoeic for a protracted period of time.

There was no suggestion that specific therapy had any effect upon the clinical course of the complicating disease in this patient. The prognosis was at any time rather poor for ultimate survival. Aplastic anaemia is a condition that generally progresses to a fatal termination despite conservative measures and blood replacement. However, careful medical management may be very productive and cases are notated which have survived for months and years. Remissions occasionally occur in the progress of the disease and are more likely in those instances where a toxic origin can be inferred. Scott, Cartwright and Wintrobe (1959) are convinced that even after years of pancytopenia, spontaneous recovery of the depressed bone marrow may represent the natural course of acquired aplastic anaemia. Our most hopeful approach to this disease at present is to maintain the patient in a state of careful equilibrium and to prevent further toxic exposure.

The terminal events in this patient's illness occurred seven months after delivery, supporting our contention that the pregnancy did not represent either a causative factor or a significant influence in the major disease. Her fatal illness of three days duration is related to a haemor-

rhagic corpus luteum cyst. It is logical to presume that this haemorrhagic process mobilized most of the patient's platelet supply to this area, further depleting her already compromised coagulation ability. The terminal episode was related to generalized mucosal haemorrhages and to a moderate degree of haemorrhage present in the cerebral cortex and subarachnoid space. Haemorrhage, and particularly intracranial bleeding, is usually the principal cause of death with this condition.

Most evidence of toxic origin in cases of aplastic anaemia must necessarily be largely circumstantial. Only the cause and effect inference of toxic exposure in the patient's history serves to suggest a specific origin. Certain substances, however, are known to produce depression of bone marrow activity and in the light of our present understanding must be incriminated as aetiological factors in the production of aplastic anaemia or pancytopenia. Among the therapeutic medications that have been related to bone marrow depression are sulphonamides, arsenicals, heavy metals, certain anticonvulsant preparations, streptomycin and chloramphenicol. Among these preparations chloramphenicol has recently received the most attention.

It has been suggested that the presence of the nitrobenzene ring in the structural formula of chloramphenicol is related to its ability to produce this toxic depression of the bone marrow. During the early years following the introduction of chloramphenicol in 1948 numerous cases of aplastic anaemia were observed in relation to the use of this drug (Dameshek and Campbell, 1952; Hargraves, Mills and Heck, 1952; Hodgkinson, 1954). At this time the preparation was considered the most single common cause of aplastic anaemia in this country and it remains a principal cause. In their analysis of aetiological agents involved in over six hundred cases of hypoplastic anaemia, as well as in their own reported series of 39 cases, Scott *et al.* (1959) consider chloramphenicol, alone or in combination with other drugs, to be the most common specific aetiological agent. In a recent report of the Subcommittee on Blood Dyscrasias of the American Medical Association Committee on Research (1958), the registry on blood dyscrasias lists chloramphenicol as the most common possible aetiological agent in 136 reported cases of pancytopenia.

The aetiology of the primary bone marrow depression in this instance cannot be established with certainty. Although a cause and effect relationship here cannot be proven, we are inclined to suspect the administration of the chloramphenicol during the early weeks of the pregnancy. Other preparations were received by the patient which have been reported as aetiological agents in bone marrow depression such as acetazolamide and sulphonamides, but their implication is much less likely. Although severe bone marrow depression is most common following prolonged use of chloramphenicol, the result is not contingent upon its prolonged use and may occur after relatively short exposures and relatively small amounts. The particular time relationship with the brief period of chloromycetin therapy involved in this patient has been observed in other instances.

Chloromycetin is a very valuable and widely-used antibiotic. The actual incidence of bone marrow depression is unquestionably very low and consideration of this complication should not militate against intelligent use of the drug. Yet it must be considered a drug which, under certain circumstances in susceptible persons, may cause a bone marrow depression with pancytopenia that frequently, as in this instance, proves fatal.

Conclusions

(1) A case of pregnancy complicated by aplastic anaemia is presented with a review of the literature.

(2) Therapeutic administration of chloramphenicol was considered the most probable aetiological factor in the reported case.

(3) There is no evidence that coexistent pregnancy alters the course of this disease or that termination of the pregnancy is beneficial.

(4) There is no acceptable evidence that pregnancy serves in any way as a conditioning or causative factor of aplastic anaemia.

(5) The primary effects of this disease upon

the course of pregnancy relate to the bleeding complications incident to thrombocytopenia.

(6) Aplastic anaemia is a rare complication of pregnancy, invoking a poor prognosis for the mother, generally not responsive to specific therapy, and probably not significantly influenced in its course by the presence of the gestation or delivery.

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CHANGES IN THE PERIPHERAL PACKED CELL VOLUME IN LATE PREGNANCY

BY

IAN COPE, M.D., F.R.C.S., M.R.C.O.G.

Royal Hospital for Women, Sydney, Australia

INVESTIGATIONS of the changes in the maternal circulation in the third trimester of normal pregnancies (Thomson *et al.*, 1938; Caton *et al.*, 1949, 1951; Gemzell *et al.*, 1954; Cope, 1958) have shown that during this period there is a fall in the plasma volume and blood volume related to the date of delivery. Cope (1958) postulated that these changes were due to a partial closure of the arterio-venous shunt in the placental bed before the onset of labour. At the same time, there is a rise in the peripheral packed cell volume and as this was related to the date of delivery, it seemed possible that the increase might be used to predict the date of delivery.

Studies on clinic patients by Kerr and Davidson (1958) and others, have shown that if iron was not given as a dietary supplement in late pregnancy, the foetal requirements were only provided at the expense of the mother, who consequently developed anaemia. The extent of this anaemia would, of course, depend upon the normal average iron intake in the mother's diet. There are therefore two factors in late pregnancy acting antagonistically on the peripheral blood picture, the changes at the arterio-venous shunt and the foetal demand for iron.

This study of the peripheral packed cell volume pattern in late pregnancy was undertaken to determine, first if a sudden increase in the peripheral haematocrit occurred which might be used to predict the date of delivery and secondly to see if iron supplements were necessary in all patients in late pregnancy.

SELECTION OF CASES

Patients were selected from two of the Antenatal Clinics at The Royal Hospital for Women, Sydney. One hundred and ten patients who were attending the clinic during the period of study, and who agreed to co-operate, were examined at about the 28th week of pregnancy and thereafter at 2-weekly intervals until delivery.

Of the 110 patients, 82 had normal pregnancies, 36 of whom received iron supplements. (The usual iron preparations used were ferrous sulphate and ferrous gluconate tablets.) Of the 28 patients who had abnormal pregnancies, 10 were complicated by anaemia (haemoglobin of less than 10 g. per cent), 12 by hypertension and/or pre-eclampsia and the others by miscellaneous conditions. Eighteen of these 28 patients received iron supplements.

METHOD

The method used to estimate the packed cell volume was the microhaematocrit capillary method using the Hawksley Microhaematocrit Centrifuge and Reader (Cope, 1959).

RESULTS

The packed cell volume changes in the normal patients receiving iron (Group A) showed a gradual increase during the 100 days before

TABLE I

Packed Cell Volume Changes in Patients with Normal Pregnancies and Receiving Iron Supplements

Duration of pregnancy (days before delivery)	100–80	80–60	60–40	40–20	20–0
Number of estimations	17	25	32	33	33
Mean	33·56	34·74	35·03	36·12	36·88
Standard deviation	2·09	2·31	2·06	1·74	2·47

delivery. No sudden increase could be detected at the 32–34 weeks period, which would allow a prediction of the date of delivery to be made. The average increase from 33·56 per cent to 36·88 per cent occurred gradually between the period 100–80 days before delivery and the period 20–0 days before delivery (Table I). These patients had been receiving iron from early pregnancy and the gradual increase in the peripheral packed cell volume could not be considered to be due to a response to recent iron therapy.

The packed cell volume changes in the normal patients who were not receiving iron (Group B) showed a slight increase from 36·56 per cent to 37·44 per cent between the period 100–80 days before delivery and the period 20–0 days before delivery. No significant increase occurred until the period within 3 weeks of delivery (Table II). The average packed cell volume at 100–80 days before delivery of Group B (36·56 per cent) was greater than that of Group A (33·56 per cent). It is probable that Group B patients were not given iron because their general health was good and they were not anaemic at the commencement of pregnancy. However, in the third trimester when foetal demands increased, these patients were not able to obtain sufficient iron from their normal diet to maintain the normal increase in the peripheral packed cell volume.

The packed cell volume changes in the abnormal cases (Group C, receiving iron and Group D, not receiving iron) are presented in Table III. In Group C patients, there was a fall and then a slight rise in the packed cell volume from 35·23 per cent to 34·4 per cent and then to 36·1 per cent when considering the periods 100–80 days, 60–40 days and 20–0 days before delivery. This occurred partly as a response to iron medication and partly as the normal terminal rise in the packed cell volume. In Group D patients, there was a fall in the packed cell volume from 36·8 per cent to 33·0 per cent between the 100–80 days period before delivery and the period 20–0 days before delivery. In these cases, patients developed complications such as ante-partum haemorrhage and anaemia developed.

TABLE II

Packed Cell Volume Changes in Patients with Normal Pregnancies and Not Receiving Iron Supplements

Duration of pregnancy (days before delivery)	100–80	80–60	60–40	40–20	20–0
Number of estimations	25	37	41	44	43
Mean	36·56	36·23	36·41	36·44	37·44
Standard deviation	2·27	2·09	2·78	2·82	2·73

TABLE III

Packed Cell Volume Changes in Patients with Abnormal Pregnancies

Duration of pregnancy (days before delivery)	100–80	80–60	60–40	40–20	20–0
Mean of patients receiving iron	35·23	34·50	34·37	35·03	36·14
Mean of patients not receiving iron	36·83	35·92	35·33	35·63	33·05

Discussion

The results of these observations direct attention to the two main factors which influence the peripheral packed cell volume in late pregnancy—the normal increase during the last 8 weeks and the extra foetal iron requirements at this time.

The changes in the peripheral packed cell volume occurred slowly and no sudden increase at a particular time, such as 32 weeks, occurred to allow for a prediction of the date of delivery. A physiological change such as a partial closure of the arterio-venous shunt at the placental site, as may be inferred from McGaughey's paper (1952) and suggested by Cope (1958) might be expected to occur gradually and the present findings support this theory. With the closure of the shunt there is a return towards normal of the abnormal features of the plasma volume/total red cell mass ratio. It is important to recognize that this change occurs, as there is this apparent improvement in the blood picture in late pregnancy which is unrelated to any therapy given for the treatment of anaemia, and which may even disguise lack of improvement.

The results in the Group B patients, who had normal pregnancies and were not receiving iron, indicate that although these patients did not show a fall in the peripheral packed cell volume, there was not as significant a rise as might be expected. These patients would have benefited by iron supplements during the third trimester.

Undoubtedly, from a therapeutic point of view, the fact that normal patients cannot provide the extra iron requirements for the foetus in the third trimester, without detriment to their own blood picture, is important. However, of equal importance is the fact that there is a normal process causing an increase in the peripheral packed cell volume at that time.

Summary

Examination of the peripheral packed cell volume changes in a series of pregnant women confirmed the fact that there is a normal increase in the peripheral packed cell volume during the third trimester. This increase occurs gradually and is of no value in predicting the date of delivery. These findings support the theory of a partial closure of the arterio-venous placental shunt before delivery.

The increase in the peripheral packed cell volume was more marked in patients who had received iron supplements. All patients, even those with an apparently adequate diet, should receive iron supplements during the third trimester of pregnancy.

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PLASMA PROGESTERONE AND PREGNANEDIOL IN HUMAN PREGNANCY, DURING LABOUR AND POST-PARTUM

BY

G. N. DESHPANDE, B.Sc.
Harmsworth Research Fellow

ANTHEA K. TURNER, B.A.
Junior Biochemist

AND

IAN F. SOMMERVILLE, M.D., Ph.D.
Director
The Endocrine Laboratory Unit

From Chelsea Hospital for Women and the Institute of Obstetrics and Gynaecology, Dovehouse Street, London, S.W.3

INTRODUCTION

THE development of micro-chemical techniques has led to a considerable advance in our knowledge of the concentration of progesterone and of related steroids in the tissues and fluids of the human body.

The progress which has been made with respect to progesterone (and the 20-hydroxy progestogens) has been the subject of a recent review (Zander, 1959). Notable contributions have been the isolation of progesterone (Salhanick *et al.*, 1952) and of the 20α (and β-)hydroxypregn-4-en-3-ones (Zander *et al.*, 1958) from placental tissue; the identification and estimation of progesterone in peripheral venous blood during late pregnancy (Zander, 1954, 1955); the study of the placental concentration of these compounds throughout pregnancy (Zander and von Munstermann, 1956) and the observation that the concentration of the hormone in umbilical vein blood is considerably higher than that of peripheral venous blood (Zander and von Munstermann, 1954; Sommerville, 1957; Aitken *et al.*, 1958).

The estimation of pregnanediol in human plasma has been the subject of a special study in this laboratory. Initially, plasma pregnanediol was estimated after administration of progesterone (Sommerville, 1952) and subsequently the steroid (5β-pregnane-3α,20α-diol) was identified and estimated in peripheral venous blood during late pregnancy (Sommerville and Deshpande, 1958a, b). A range of values for plasma pregnanediol concentration throughout pregnancy was then determined in a series of healthy women (Deshpande and Sommerville, 1958). Comparison of these values with those previously reported for plasma progesterone in late pregnancy (Zander, 1954, 1955; Sommerville, 1957; Short, 1958), indicated that it would be of interest to study the progesterone/pregnanediol ratios in pregnancy plasma and to carry out a consecutive series of analyses in individual pregnancies. The present report is concerned with this aspect of the work and describes the results obtained during the third trimester of pregnancy,

during labour and immediately post-partum. In addition, analyses were carried out upon placental tissue and umbilical vein blood. This project has been the subject of a preliminary report (Sommerville, 1960).

Methods

For the estimations in plasma the method of Sommerville and Deshpande (1958b) was employed, with the addition of a paper chromatographic step for the further purification of the progesterone fraction. In the original method this step was used to test the purity of the final product, whereas in the present series it was incorporated in each assay. The paper chromatographic technique is similar to that previously employed (Zander and Simmer, 1954) but progesterone was located on the paper strips by the application of dinitrophenylhydrazine reagent. The estimation of plasma pregnanediol was carried out without modification.

Experimental details of the additional step are as follows: the five eluates of 20 per cent chloroform in n-hexane are pooled, evaporated to dryness, the extract redissolved in pure methanol and applied to a paper strip (1 cm. × 50 cm.). The filter paper (Whatman No. 1) is pre-washed with 70 per cent methanol for 48 hours. Pure authentic progesterone is applied to another strip. The solvent system consists of n-hexane and aqueous methanol (85 per cent) in equal proportions. The chromatogram is inserted into the chromatographic tank, which is placed in a thermostatically controlled box (95° F.) for an equilibration period of three hours. At the end of the equilibration period the mobile phase (n-hexane) is added and the chromatogram is run for one hour. It is then taken out and dried in air. The standard strip is developed with a saturated solution of dinitrophenylhydrazine in 0·1N HCl. The hydrazone appears within ten minutes as an orange yellow spot. A corresponding area is removed from the strip to which the extract was applied and this is eluted with methanol (analytical reagent, redistilled). The eluate is evaporated to dryness under negative pressure, redissolved in n-hexane and a second chromatogram is carried out upon alumina as in the original method. In order to investigate possible losses due to introduction of the additional step, recovery experiments were carried out in which 2 μg. to 6 μg. of progesterone was added to 10 ml. samples of male plasma. The recoveries fell within the range 70–80 per cent. This is approximately 10 per cent lower than recoveries by the original method (which yielded 80–95 per cent recovery of progesterone or pregnanediol from male plasma), but the incorporation of the additional step was considered desirable in view of the increased purification of the progesterone fraction.

Placental progesterone was estimated by the method of Zander and Simmer (1954). This was, however, modified by the addition of two of the features of the method of Sommerville and Deshpande. Thus the progesterone eluted from the paper chromatogram was re-chromatographed on an alumina column and was then estimated quantitatively as the iso-nicotinic acid hydrazone (Sommerville and Deshpande, 1958b).

Materials and Results

Consecutive assays were carried out upon a series of 13 women (aged 19–35 years). In one subject there was the history of a previous miscarriage (Subject 3) and the remainder were primigravidae. In all cases the course of pregnancy had been uncomplicated up to the onset of the investigation. In three cases, however (Subjects 3, 7 and 10), Caesarean section was performed for prolonged labour and in a further case (Subject 8) spontaneous delivery did not occur until the 43rd week. The stage of pregnancy, expressed in weeks, was based upon the conventional calculation from the date of the last menstrual period. The peripheral venous blood (15–20 ml.) was collected from the cubital vein, and heparin was added to prevent clotting. With the exception of samples collected during labour and post-partum, the venepuncture was performed between 9.30 a.m. and 11 a.m. Samples of umbilical vein-blood were drawn from the veins by syringe immediately after the delivery of the placenta. The plasma was separated by centrifugation within one hour of collection, and extraction was carried out without delay.

Four subjects were studied in the last trimester of pregnancy (Subjects 1 to 4) and the results of the assays are illustrated in Figures 1 to 4. In the figures, the progesterone concentration is indicated by solid lines and the pregnanediol concentration by interrupted lines. Delivery is indicated by an arrow.

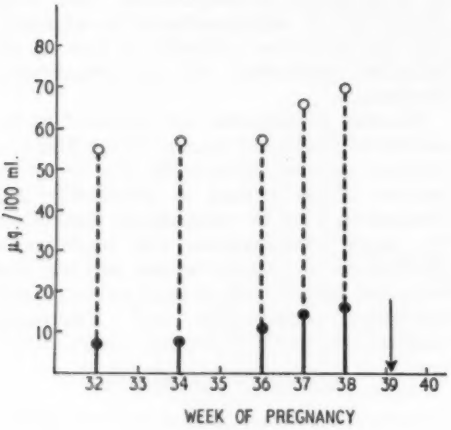

FIG. 1

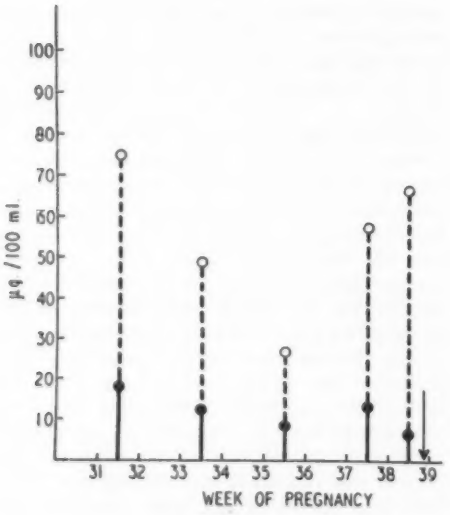

FIG. 2

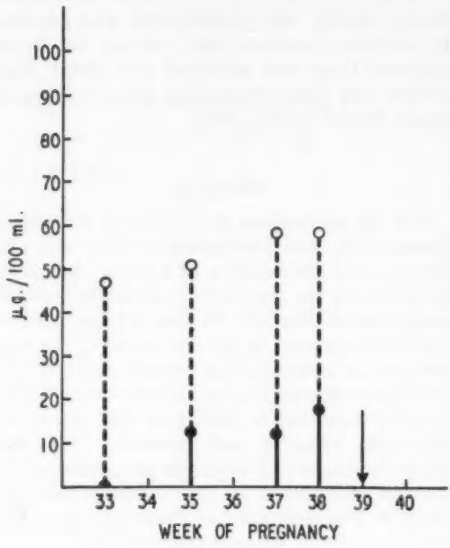

FIG. 3

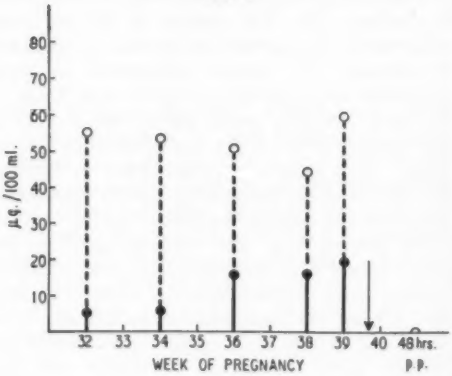

FIG. 4

In addition, four subjects were studied in the third trimester, during labour and post-partum. The details and results are shown in Table I and Figures 5 to 8. The assays indicated in the figures as post-partum date from the time of delivery of the infant and the time which elapsed after the delivery of the placenta can be calculated from the duration of the third stage of labour.

TABLE I

Case No.	Name	Age	Duration of Labour: Stage			Plasma Progesterone Cord Blood μg./100 ml.	Plasma Pregnanediol Cord Blood μg./100 ml.	Placental Progesterone μg./g. Wet Tissue	Comment
			1st	2nd	3rd				
5	J.L.	32	30 hours 5 minutes	1 hour 10 minutes	5 minutes	69·0	*	1·42	Normal delivery
6	E.S.	33	15 hours	1 hour	15 minutes	83·3	57·2	0·99	Normal delivery
7	J.A.	25	31 hours 5 minutes	—	5 minutes	23·7	86·0	0·90	Caesarean section for prolonged labour
8	V.N.	19	4 hours 35 minutes	50 minutes	5 minutes	53·4	*	0·89	Breech delivery

* Not assayed.

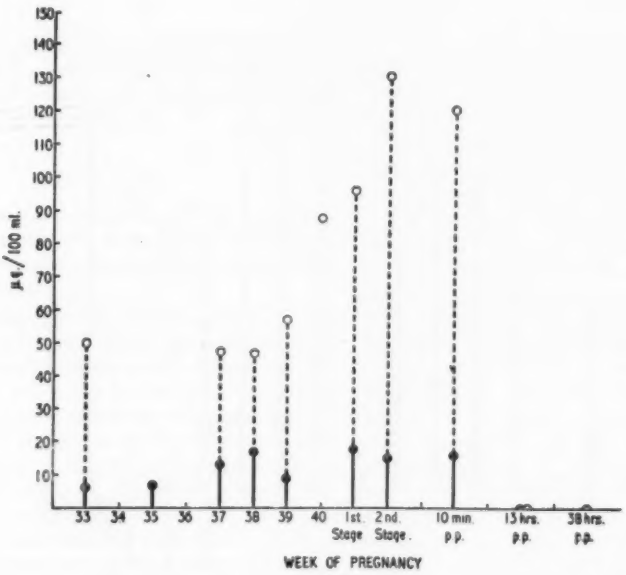

FIG. 5

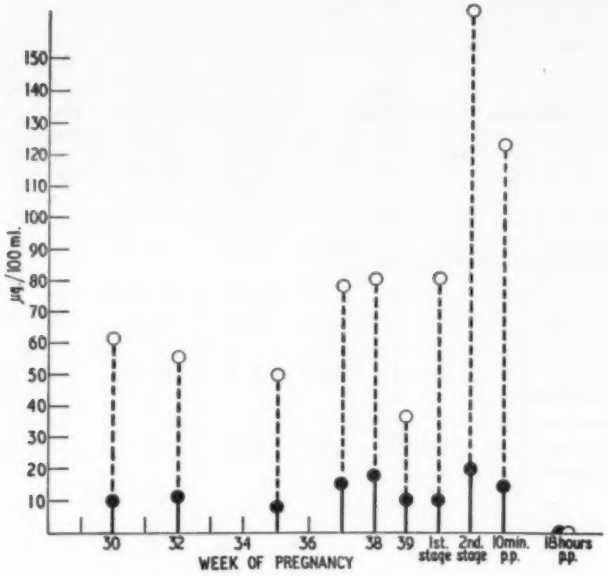
µg./100 ml.
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
30
32
34
36
38
39
1st. stage
2nd. stage
10min. p.p.
18hours p.p.
WEEK OF PREGNANCY

FIG. 6

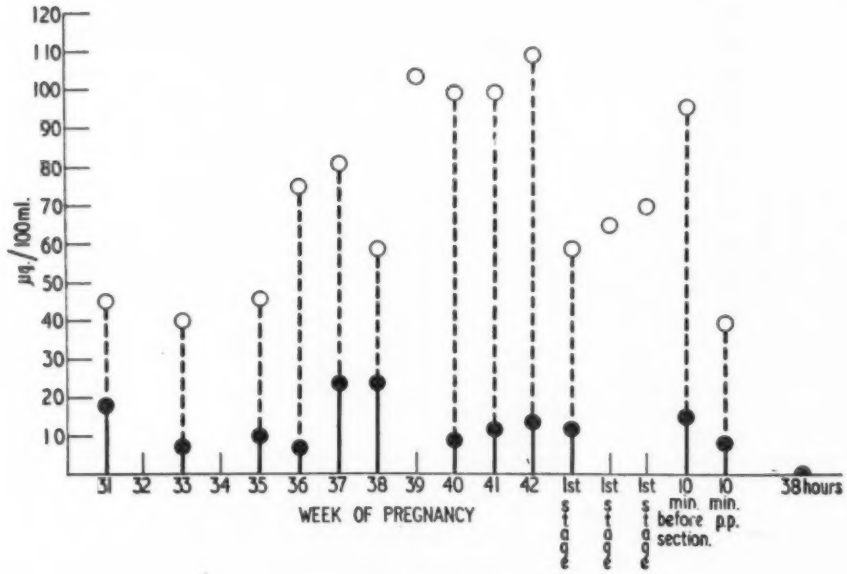
µg./100ml.
120
110
100
90
80
70
60
50
40
30
20
10
31
32
33
34
35
36
37
38
39
40
41
42
1st stage
1st stage
1st stage
10 min. before section.
10 min. p.p.
38hours
WEEK OF PREGNANCY

FIG. 7

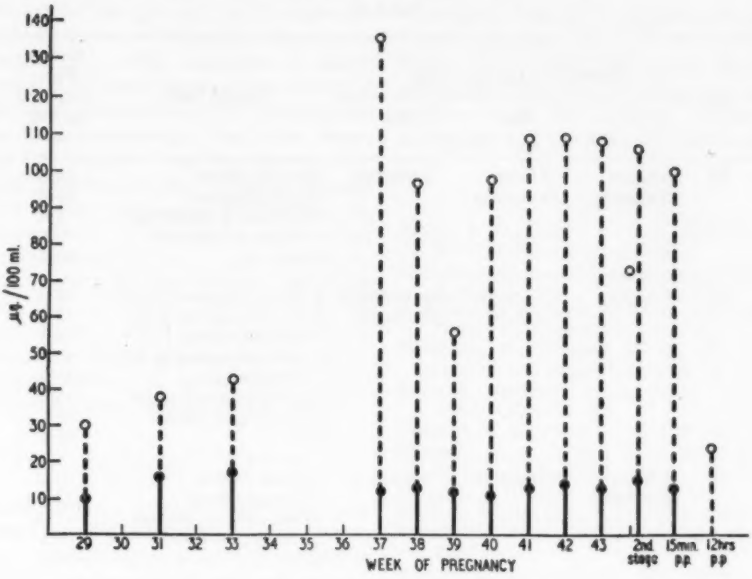

FIG. 8

In view of the results observed in labour in Subjects 5 to 8, a further 5 subjects were investigated during labour and post-partum. The results are given in Table II.

DISCUSSION

The work is still in progress. It is not proposed, therefore, to attempt to draw general conclusions at this time, but the following facts emerge from the present study:

(a) *Peripheral venous blood:* There is no evidence of a fall in plasma progesterone concentration in late pregnancy or in labour. On the contrary, there is a rise in the concentration in 4 of the 8 subjects in whom relevant data was obtained. Information in the literature upon this point is confined to the study of random plasma samples, and while a pre-labour rise in the progesterone values was recently observed in one group of assays (Short and Eton, 1959), it was not observed in a previous study (Zander, 1955, 1959). Similarly the plasma pregnanediol concentration does not show a marked fall until after delivery of the placenta and, in addition, it will be observed that markedly elevated values occur either before or during labour. It is of especial interest to note that this rise in plasma pregnanediol concentration is frequently unaccompanied by a proportionate rise in the concentration of the hormone. Thus, whereas the mean progesterone/pregnanediol ratio between the 29th and 35th weeks of pregnancy is of the order of 1:4, ratios of 1:8 or even 1:14 were obtained in the later samples. Figure 8 illustrates the change in ratio which occurred several weeks before the onset of labour in a subject, who was not receiving drugs nor subject to the stress of parturition. It is too early, however, to assess the possible importance of these factors. It will be of considerable interest to investigate the basis of this phenomenon, which may reflect a shift in the metabolism of the hormone and may be relevant to the physiological mechanism of labour.

TABLE II

Case No.	Name	Age	Duration of Labour: Stage			Sample Taken	Plasma Progesterone μg./100 ml.	Plasma Pregnanediol μg./100 ml.
			1st	2nd	3rd			
9	N.H.	20	18 hours 30 minutes	2 hours 13 minutes	2 minutes	1st stage labour	13·1	159·2
						2nd stage labour	14·4	200·0
						10 minutes post-partum	5·8	82·8
						17 hours post-partum	Nil	Nil
						Cord	40·4	51·7
10	B.B.	29	48 hours	Caesarean section	Approximately 20 minutes	6 days pre-partum (p.m.)	15·3	111·5
						6 days pre-partum (a.m.)	12·0	123·5
						3 days pre-partum (a.m.)	9·1	163·0
						3 days pre-partum (p.m.)	13·6	190·0
						1st stage labour	14·4	175·0
						20 minutes post-partum	13·3	226·0
						22 hours post-partum	Nil	49·4
						Cord	46·8	116·0
11	A.A.	31	10 hours 50 minutes	30 minutes	5 minutes	1st stage labour	23·2	80·0
						2nd stage labour	33·2	112·3
						10 minutes post-partum	17·2	71·3
						17 hours post-partum	Nil	33·0
						Cord	94·3	68·0
12	B.B.	27	11 hours 30 minutes	1 hour 35 minutes	20 minutes	4 days pre-partum (p.m.)	11·9	54·1
						3 days pre-partum (a.m.)	12·9	58·1
						1st stage labour	10·7	45·9
						2nd stage labour	25·9	112·0
						20 minutes post-partum	9·6	32·1
						Cord	88·0	147·0
13	D.I.	22	13 hours 25 minutes	40 minutes	10 minutes	1st stage labour	Not detected	129·5
						2nd stage labour	21·0	162·0
						15 minutes post-partum	13·0	86·8
						1 hour post-partum	Nil	70·0
						Cord	128·5	69·0

(b) *Placental tissue and umbilical vein blood:* In this series, plasma progesterone concentration in placental tissue falls within the range previously reported (Zander and von Münstermann, 1956) and the progesterone assays in umbilical vein blood confirm and extend the results of previous work (Zander and von Münstermann, 1954; Sommerville, 1957; Aitken *et al.*, 1958). The observation in umbilical vein blood of pregnanediol concentrations of from 51·7 μg. to 147·0 μg. per 100 ml. plasma is a new finding of especial interest. This range of values in foetal blood is comparable with that in the peripheral venous blood of the mother and suggests several possibilities. Pregnanediol, derived from the metabolism of the hormone by maternal tissue (and this may include metabolism within the placenta), may be transferred across the placental membrane. On the other hand, the observation may reflect steroid secretion and metabolism within the foetus. Reduction of progesterone in the C_{20} position by placental homogenates has been demonstrated (Little *et al.*, 1959) and, as noted in the introduction, the reduction products have been isolated from human placentae (Zander *et al.*, 1958). There is

also evidence for the presence of 3α-hydroxysteroid dehydrogenase in placental microsomes (Meigs and Engel, 1958). Attempts to detect pregnanediol in placental tissue in the course of the present work were unsuccessful, but technical difficulties were encountered. Two other observations in the literature may be relevant. The first is that pregnanediol has not been detected in the urine of the newborn (de Watteville *et al.*, 1951; Zander and Solth, 1953), even after progesterone administration (Zander and Solth, 1953); the second is that studies upon the metabolism of oestrogens in the newborn (Diczfalusy *et al.*, 1957) and of oestrogen concentrations in foetal plasma (Aitken *et al.*, 1958) suggest differences in oestrogen metabolism between foetal and maternal tissues.

Summary

A method for the quantitative determination of progesterone and pregnanediol in human plasma has been applied in a series of women in late pregnancy, during labour and post-partum (201 estimations by the method of Sommerville and Deshpande, 1958b). The plasma concentrations are illustrated and discussed. It is found that a change in the progesterone/pregnanediol ratio occurs in a proportion of samples collected before, or during labour. Plasma pregnanediol was determined in umbilical vein blood and the range of values was similar to that observed in the maternal circulation.

Acknowledgments

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FURTHER OBSERVATIONS ON THE SAFETY OF THE PITOCIN DRIP

BY

T. J. RYAN, M.R.C.O.G.
Research Fellow
Gynaecological Research Department, Queen Elizabeth Hospital, Gateshead

IN a previous paper (Ryan, 1958) on the use of the pitocin drip for the induction of labour the author analyzed a personal series of 323 patients. The present paper describes its use in a further 327 patients, and the form of analysis will be similar to that used in the earlier paper. As before, there was no maternal death or ruptured uterus.

The series consisted of two groups.

GROUP A: USE OF THE PITOCIN DRIP IN PATIENTS IN WHOM THE ONSET OF LABOUR WAS DELAYED MORE THAN 24 HOURS AFTER MEMBRANE RUPTURE

This comprised 227 patients of whom 90 were primigravidae and 137 multiparae. There was no selection of patients and the duration of gestation was:

18 weeks: 1 patient	35 weeks: 3 patients
22 weeks: 1 patient	36 weeks: 6 patients
30 weeks: 1 patient	37 weeks: 13 patients
31 weeks: 1 patient	38 weeks: 25 patients
32 weeks: 1 patient	39 weeks: 23 patients
34 weeks: 3 patients	40 weeks: 48 patients
	Over 40 weeks: 101 patients

METHOD

One-quarter ml. (2·5 units) of pitocin was *thoroughly* mixed with 1 bottle (540 ml.) of dextrose, dextrose in saline or normal saline, and the drip was started and run at the rate of approximately 40 drops per minute.

There was no constant supervision of the patient, who was seen only as often as one undergoing normal labour, *and this I regard as the cardinal point in my 2 papers on the subject.*

RESULTS

Two hundred and fourteen patients (94 per cent) were delivered within 36 hours of the commencement of the drip, the average time between commencement of the drip and establishment of labour (latent period) being 1 hour 30 minutes for multiparae and 3 hours for primigravidae; in fact in only 5 of the successes did the latent period exceed 12 hours (26 hours, 12¼ hours, 24 hours, 23 hours, 13 hours). The average length of labour was 5 hours 45 minutes for multiparae, 9 hours 50 minutes for primigravidae, although in 8 patients labour was prolonged beyond 24 hours (25 hours, 27¼ hours, 25¾ hours, 29¼ hours, 28½ hours, 24½ hours, 28¾ hours, 29½ hours). The average amount of pitocin used was 4·1 units for multiparae and 8·6 units for primigravidae.

Of the 13 patients on whom the method was not successful details are given in the appendix.

Method of Delivery of 228 Infants (including 3 Sets of Twins and Excluding the 2 Abortions)

In 174 cases this was as a spontaneous vertex, in 10 cases as an assisted breech, in 34 cases as forceps, in 1 case as a breech extraction, and in 9 cases by Caesarean section. Regarding the Caesarean sections 2 were performed for dis-

proportion after adequate trials of labour, 2 were performed because of prolapsed cord, and 5 were performed as a result of failure of the method of induction.

Outcome to 228 Infants

There were 10 stillbirths and 4 neonatal deaths. Details of the stillbirths are as follows: 2 were dead before induction was commenced, 2 were anencephalics, 1 was born dead as a result of a badly executed breech delivery, and 2 weighing respectively 3 pounds 14 ounces and 3 pounds 12 ounces were born to mothers with severe pre-eclampsia.

The remaining 3 stillbirths necessitate a fuller report:

Para-0+1. 36 weeks. Pre-eclampsia. Membranes were artificially ruptured and 28 hours later labour had not commenced. Drip was started and after 18¾ hours labour began during which a temperature of 102° was recorded due to uterine infection. Labour lasted 24 hours and resulted in the spontaneous delivery of a 5 pounds 14 ounces fresh stillborn infant. The foetal heart rate was 132 per minute immediately before birth.

This death was, I believe, due to a combination of sepsis, toxaemia and long labour, and I do not believe that the pitocin drip can be implicated as a causative factor in the death.

Primigravida. Aged 33. Spontaneous rupture of membranes at 38 weeks. Twenty-six hours later labour had not begun and the drip was started. Labour commenced 1½ hours later and an hour later the drip needle blocked and the drip was taken down. Labour continued and half an hour later the foetal heart ceased abruptly. The contractions had never been tumultuous or overfrequent. Two hours later the drip was recommenced and after a further 2 hours a fresh stillborn infant weighing 5 pounds 3 ounces was delivered spontaneously. The placenta was small and markedly infarcted.

This death was I believe due to placental insufficiency.

Para-1. Previous Caesarean section because of a double headed monster. Spontaneous rupture of membranes at 38 weeks. Thirty-six hours later I examined her and found a ripe cervix. I returned half an hour later and started a drip, although told by the attendant midwife that labour had started spontaneously. The drip rate was approximately 60 drops per minute and this labour was turbulent, resulting in a foetal death at full dilatation.

This death was due to the pitocin drip and its use on this patient was due simply to haste and carelessness.

Of the 4 neonatal deaths, 2 were abnormal babies, 1 was an assisted breech of a second twin weighing 3½ pounds which lived 15 minutes. The last baby weighed 3 pounds 12 ounces and died of acute pericarditis on the 5th day.

Group B: Artificial Rupture of Membranes Combined with Pitocin Drip

In certain obstetric complications it is deemed advisable that labour should commence as soon after induction as possible. These complications include eclampsia, severe pre-eclampsia, concealed accidental haemorrhage, unstable lie, minor degrees of placenta praevia, intrauterine death, and meconium staining in the liquor as revealed at artificial rupture of the membranes.

In these patients artificial rupture of the membranes was performed and a pitocin drip exhibited almost immediately after. The dosage and care of the drip were as for the patients in Group A.

There were 100 patients consisting of 66 multiparae and 34 primigravidae. The duration of gestation was:

18 weeks: 1 patient	34 weeks: 1 patient
23 weeks: 1 patient	35 weeks: 2 patients
26 weeks: 1 patient	36 weeks: 6 patients
27 weeks: 1 patient	37 weeks: 8 patients
29 weeks: 1 patient	38 weeks: 14 patients
31 weeks: 1 patient	39 weeks: 19 patients
32 weeks: 4 patients	40 weeks: 19 patients
33 weeks: 2 patients	Over 40 weeks: 19 patients

Results

Ninety-six patients (96 per cent) were delivered within 36 hours, the average latent period being 2 hours for multiparae and 1 hour 40 minutes for primigravidae. This compares very favourably with 70 per cent of patients delivered in the 36 hours following artificial rupture of the membranes alone.

The average length of labour was 5 hours 40 minutes for multiparae and 11 hours 5 minutes for primigravidae: in only 2 of the successes was labour prolonged beyond 24 hours (24½ hours, 25 hours).

The average amount of pitocin used was 6 units for multiparae and 8 units for primigravidae.

Details of the 4 failures are given in the appendix.

Method of Delivery of 97 Infants (including 1 Set of Twins and excluding the Four Abortions)

In 71 cases this was as a spontaneous vertex, in 7 as an assisted breech, in 15 by forceps extraction and in 4 cases by Caesarean section because of failure of the method of induction.

Outcome for 97 Infants

There were 14 stillbirths and 5 neonatal deaths. Of the stillbirths, 9 were dead before induction was started, 3 were abnormal babies, 1 was the result of a badly executed breech delivery and a 3-pounds baby was delivered to a mother with severe toxaemia.

Of the neonatal deaths, 1 died during exchange transfusion, 1 weighing 4 pounds 11 ounces died at 7 hours (the mother had placenta praevia), and the other 3 were born to mothers with severe pre-eclampsia (a 3-pounds baby dying at 32 hours, a 5-pounds 6-ounces baby dying at 56 hours and a 3-pounds 6-ounces baby dying at 2 hours).

Discussion

To Supervise or Not to Supervise?

Constant supervision of a patient having a pitocin drip is time consuming and unnecessary. The protagonists of constant supervision continually teach that this must be by a qualified obstetrician or midwife. In their practice this duty devolves on a medical student or pupil midwife.

The Physiological or Pharmacological Drip

Theobald, whose opinion merits serious thought, makes great issue regarding the physiological as opposed to the pharmacological drip, maintaining that the latter is both unnecessary and dangerous. However, in his most recently reported series (Theobald, 1959) of 295 patients on whom he used the drip in doses from ½ to 2 units per 540 ml. at between 20 and 40 drops per minute, 16 per cent were not delivered within 36 hours and the Caesarean section rate was 14 per cent. I submit that had he used a higher dosage his figures would, without hazard to mother or foetus, have been improved.

As it is, at the moment, impossible to know the precise dosage for any specific patient a general idea of efficient dosage is needed. We believe this efficient dosage to be 2·5 units per 540 ml. at approximately 40 drops per minute continued throughout labour. The drip was often slowed to about 20 drops per minute towards the end of the first stage. We have observed that, when the drip rate was less than 20 drops per minute, 20 per cent of the patients had either a long latent period or a long labour.

What are the Reservations About the Use of the Drip?

We believe that it is safe to use the drip on any patient for whom induction of labour seems necessary, and, contrary to the advice of many critics, have used it in the present series on the following:

	Patients
Pre-eclampsia and essential hypertension	85
Disproportion	9
Previous Caesarean section	10
Elderly primigravidae (35 years and over)	6
Grand multiparae (1: para-11; 1: para-9; 2: para-8; 4: para-7; 5: para-6)	13
Concealed accidental haemorrhage	4
Eclampsia	1
Twin pregnancy	4
Unstable lie	12

and on 4 multiparae who had no previous living children, 3 patients with meconium-stained liquor and 1 patient in whom the foetal heart was irregular before the membranes were ruptured. These last 8 all delivered living children vaginally.

Acknowledgments

Two hundred and sixty-two patients were under the care of Miss J. E. Bottomley and Mr. O. Lloyd at the Cambridge Maternity Hospital. The remaining 65 patients were under

the care of the Consulting Obstetricians at the Newcastle General Hospital, Mr. Linton Snaith, Miss D. Kerslake and Mr. Hugh Arthur.

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Appendix

Details of the 13 failures in Group A.

(1) Para-0, 37 weeks. Thirty-six hours of pitocin drip resulted in no labour. Caesarean section.

(2) Para-0, 42 weeks, unripe cervix. Latent period ¾ hour, 23-hour inefficient labour resulted in a Caesarean section.

(3) Para-0, 41 weeks, unripe cervix. A 21-hour inefficient labour resulted in a Caesarean section.

(4) Para-0+1, 36 weeks, unripe cervix. After 18¾ hours of drip labour started and during a 24-hour labour intra-uterine infection occurred resulting in a stillborn infant.

(5) Para-0, 42 weeks, breech, unripe cervix. Drip started and half an hour later an inefficient labour began, resulting 24 hours after in a Caesarean section.

(6) Para-0, 37 weeks, cartilaginous cervix. Labour had not commenced after six bottles of the drip. Caesarean section.

(7) Para-0, 37 weeks, unripe cervix. Twenty-six hours of drip resulted in hypotonic inertia and spontaneous delivery 28 hours later of a living infant.

(8) Para-0, 42 weeks, unripe cervix, 24 hours of drip at standard dosage resulted in no labour. Dosage doubled, labour commenced immediately and 5 hours later a living infant was delivered by forceps.

(9) Para-1, 38 weeks. Latent period 9½ hours, labour 34 hours. Spontaneous delivery living infant.

(10) Para-1, 42 weeks, unripe cervix. Seven bottles of drip at standard dosage did not produce labour. Dosage doubled. Labour commenced immediately, lasted 11¼ hours and resulted in spontaneous delivery of living infant.

(11) Para-4, 38 weeks, unripe cervix. Latent period 25½ hours, labour 13 hours, spontaneous delivery of living infant.

(12) Para-4, 38 weeks, unripe cervix. Six bottles at standard dosage produced no labour. Dosage doubled. Four hours latent period and 2¼-hour labour. Living infant.

(13) Para-3, 42 weeks, unripe cervix. Six bottles at standard dosage produced no labour. Drip stopped. Restarted next day. Labour commenced immediately, lasted 2 hours. Living infant.

Details of the 4 failures in Group B.

(1) Para-0, 40 weeks, unripe cervix. Latent period 1½ hours, inefficient labour for 21 hours. Caesarean section.

(2) Para-0, 40 weeks, ripe cervix. Twelve hours of drip failed to institute labour. In view of age (40) Caesarean section.

(3) Para-2, 39 weeks, unripe cervix, unstable lie. Six hours drip produced no labour. Lie still unstable. Caesarean section.

(4) Para-3, 37 weeks, unripe cervix, unstable lie. Twenty-one hours of drip failed to produce labour. Transverse lie. Caesarean section.

THE RESPONSE OF THE BULBAR CONJUNCTIVAL VASCULAR BED TO HUMORAL STIMULI

BY

DEREK TACCHI, M.B., M.R.C.O.G.*

From the Department of Obstetrics and Gynecology, College of Medicine, University of Illinois, Chicago

THE anatomy and physiology of the capillary circulation have been well documented and in man the bulbar conjunctiva provides an excellent field for its study (Ruedeman, 1933; Zweifach, 1949; Bloch, 1954). Since the pioneer work of Knisely and Bloch in 1945, observers of the conjunctival vascular bed have reported functional changes in all its components during menstruation, ovulation, normal pregnancy and in the toxaemias of pregnancy (Zilliacus, 1950; Landesman *et al.*, 1953a, b, 1954). At these times of physiological change, when there is a known variation in blood hormone levels, vasoconstriction appears in the capillary bed. The implication of such findings depends upon the assumption that the vascular changes observed in the conjunctiva represent a similar process occurring throughout the entire capillary bed. Hallum (1947), Zilliacus (1950) and Bloch (1954) feel that this is a reasonable assumption.

The changes in the peripheral blood vessels observed in toxaemia of pregnancy are thought to be part of a generalized arteriolar spasm and Hertig (1945) has demonstrated histopathological changes in the pre-capillary arterioles of a variety of organs. Vasoconstriction in the capillary bed may be produced by a neurogenic or a humoral stimulus and in pregnancy toxaemia the humoral factor probably predominates (Govan *et al.*, 1951; Assali, 1954). Investigation of the response of the peripheral vascular bed to humoral stimuli may help in the continued search as to the true nature of pregnancy toxaemia.

Lee and Holze (1950) and later Landesman *et al.* (1953a) described a method of recording their observations of the bulbar conjunctival vascular bed photographically. Using a similar technique I have observed the effects of certain steroid hormones, administered locally and parenterally, on the conjunctival vascular bed.

METHODS

In all studies a standard Poser slit-lamp with paired 40 mm. objectives and paired wide-angled eyepieces (15×) was used. A 35 mm. single lens reflex camera with f/2 lens and penta-prism eye level viewfinder was fitted to the barrel of one of the eyepieces. Illumination was from an electronic flash unit of 100-watt seconds output at a distance of 12 inches from the eye. Kodak, black and white, Plus-X, panchromatic film, A.S.A. 80, was used with a lens setting of f/5·6 and an exposure time of 1/50th second synchronized with the electronic flash on the X setting.

The subject was made comfortable in the head rest and chin cup with her eyes directed to one side at an angle of 60 degrees. With practice, fixation could be held for up to 5 minutes. Using direct focal illumination, adjustment of the slit control produced a sharply defined area of surface illumination. The conjunctiva was scanned and a suitable area, which could be recognized at a subsequent examination, was selected. This field was observed through the

* Present address: General Hospital, Newcastle upon Tyne 4.

camera viewfinder and the exposure made at the moment the vessels were in sharp focus.

The *sensitivity* of the arterioles was determined by dropping epinephrine solution into the conjunctival sac in strengths varying from 1/10,000 to 1/40,000.

Local Administration

The human eye lends itself to the surface application of drugs. The conjunctiva is covered by a thin epithelium which allows pharmacological agents to diffuse readily across it and induce responses in the vessels. Steroids are not water soluble. Therefore most ophthalmic instillations containing steroids are in the form of suspensions. It was difficult to obtain true solutions. Five per cent propylene glycol could be used as the solvent for hydrocortisone and a steroid antagonist Spirolactone (SC 8109) in strengths of 100 gamma per ml. Progesterone and desoxycorticosterone acetate, 50 gamma per ml., were dissolved in isotonic 10 per cent propylene glycol. Preliminary control instillations of isotonic 5 and 10 per cent propylene glycol solutions showed that they had no effect on the conjunctival vascular bed. Oestrone sulphate was obtained as a 0·5 per cent solution in isotonic saline.

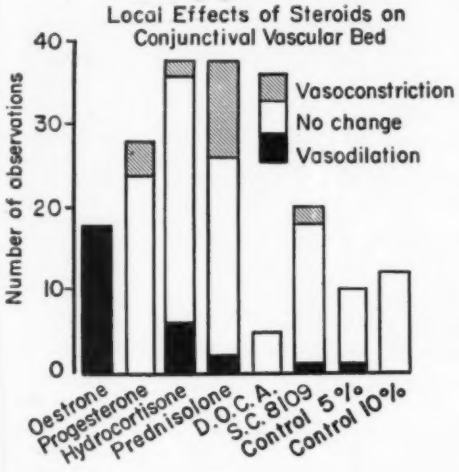

FIG. 1

Five normotensive nulliparae aged 22 to 30 years were the subjects in this investigation. The selected area of conjunctiva was first observed and photographed. Two drops of the solution to be tested were placed in the conjunctival sac and the eyelid closed for 15 seconds. This procedure was repeated, after which the conjunctiva was again observed and photographed. The epinephrine sensitivity was determined before and after each instillation but in no instance was any change observed. Instillations were made at various times during the menstrual cycle and a good scatter was obtained. The results are shown graphically in Figure 1.

Comment

As all photographs were taken with identical camera and light settings, direct comparisons could be made from them. After instillation of the oestrone solution, slight vasodilatation was observed in all subjects (Figs. 2 and 3) and when prednisolone was used slight vasoconstriction was observed in one-third of them (Figs. 4 and 5). With the remaining drugs no significant effect was observed. In addition to the normal women, 5 pregnant patients with toxaemia each had instillations of SC 8109 during the third trimester. No change was observed in the capillary bed of any of them.

Parenteral Administration

Twenty-seven patients of varying age and parity both with and without functioning ovaries were studied. Three preparations were used:

(1) A water soluble conjugated oestrogen ("Premarin") which was given by intravenous injection in doses of 20 to 40 mg.

(2) Progesterone ("Proluton") which was given by intramuscular injection in doses of 100 mg.

(3) Testosterone proprionate ("Perandren") which was given by intramuscular injection in doses of 50 mg.

TABLE I

Summary of Patients Given Intravenous Oestrogen

Number	Age	Parity	Day of Cycle	Dose of Oestrogen mg.	Observed After		Effect on Capillary Bed
					Hours	Minutes	
1 ..	35	1	2nd	20	2	0	dilatation
2 ..	35	1	6th after castration	20	2	0	dilatation
3 ..	38	9	15th	20	1	0	no change
4 ..	25	7	2nd	20	0	45	dilatation
5 ..	26	0	menorrhagia	40+ oral 75	24	0	dilatation
6 ..	39	10	21st	40	1	30	no change
7 ..	39	0	primary amenorrhoea	40	1	0	dilatation
8 ..	39	0	10th	40	1	0	no change
9 ..	39	0	28th	40	2	0	dilatation
	39	0	28th	40	18	0	dilatation
10 ..	39	0	6th after castration	40	0	30	dilatation
11 ..	55	2	post-menopausal	40	2	0	no change
12 ..	34	5	8th	40	2	0	no change
13 ..	45	0	3rd	40	3	45	dilatation
14 ..	39	0	previous hysterectomy	40	3	45	dilatation
15 ..	18	2	13th	40	2	30	no change
	18	2	13th	40	21	0	no change
16 ..	19	0	14th	40	4	30	no change

TABLE II

Summary of Patients Given Intramuscular Progesterone

Number	Age	Parity	Day of Cycle	Dose of Progesterone mg.	Observed After	Effect on Capillary Bed
					Hours	
1	44	5	20th	100	2	no change
	44	5	20th	100	18	reduction
2	35	3	post-operative 7 days	100	4	reduction
3	39	0	primary amenorrhoea	100	2	no change
	39	0	primary amenorrhoea	100	26	no change
4	37	3	16th	100	22	dilatation
5	31	3	5th	100	22	no change
6	53	1	castrated 14 years	100	19	no change
7	56	5	menopausal 7 years	100	23	no change
8	34	2	6th	100	23	reduction
9	42	7	radium castration	100	21	reduction

TABLE III

Summary of Patients Given Intramuscular Testosterone

Number	Age	Parity	Day of Cycle	Dose of Testosterone mg.	Observed After	Effect on Capillary Bed
					Hours	
1	42	1	20th	50	22½	no change
2	25	2	26th	50	24	no change

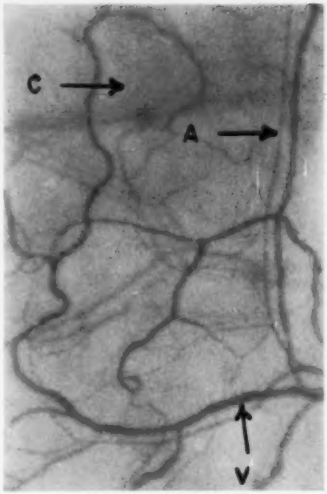

FIG. 2

B.K. Day 29 of 31 day cycle. Normal vascular bed. ×50. A=Arteriole. B=Venule. C=Capillary Bed.

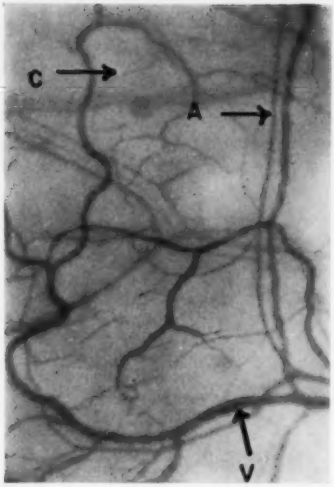

FIG. 3

B.K. Following oestrone instillation. Dilatation of all elements of vascular bed. ×50.

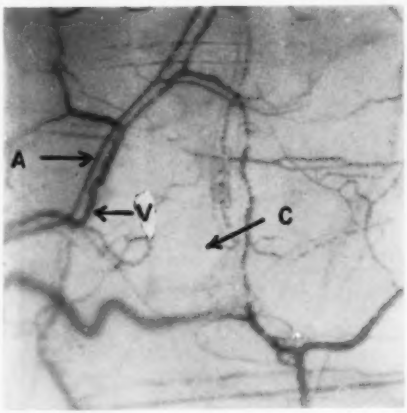

FIG. 4

A.A. Day 20 of 28 day cycle. Normal vascular bed. ×50.

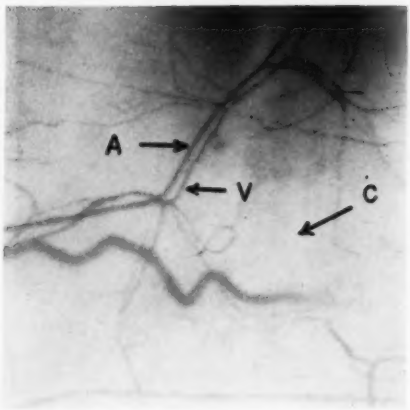

FIG. 5

A.A. Following prednisolone instillation. Reduction of all elements of vascular bed. ×50.

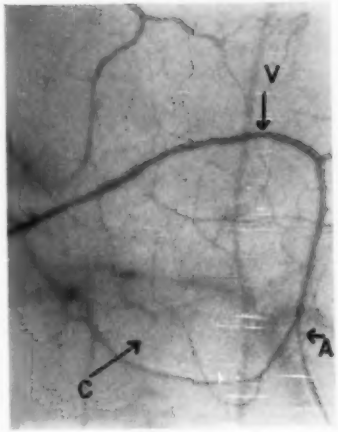

FIG. 6
C.S. Day 28 of 29 day cycle. Premenstrual vascular bed. ×50.

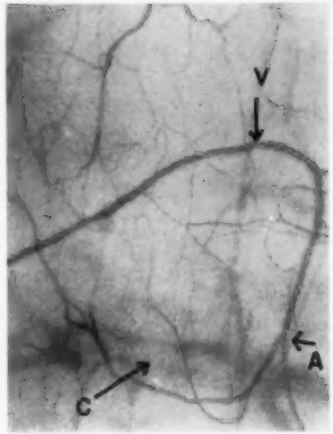

FIG. 7
C.S. Forty-five minutes after intravenous oestrogen. Dilatation of capillary bed. ×50.

In each subject prior to the administration of the selected preparation the conjunctival bed was observed and photographed. The injection was then given and repeat observations were made at times varying from 30 minutes to 24 hours later. The findings are summarized in Tables I, II and III.

Comment

After the intravenous injection of oestrogen the capillary bed showed slight dilatation in 9 instances and no change in 7. In the former group, 4 patients were menstruating, one was immediately premenstrual, 3 had been surgically castrated and one had primary amenorrhoea. In the latter group 6 patients were between the eighth and twenty-first days of their menstrual cycle and one was post-menopausal. The most marked response, shown in Figures 6 and 7, was in a 39-year old nulligravida on the 28th day of her cycle.

After an intramuscular injection of progesterone a reduction of the capillary bed was observed in 4 patients, dilatation in one and no change in the remaining 4.

In the 2 patients studied after an intramuscular injection of testosterone there was no change observed.

Discussion

Local instillation of oestrone was followed by slight vasodilatation of the capillary bed on each occasion. With prednisolone slight vasoconstriction was observed in about 30 per cent of the subjects. The lack of response to instillation of the other steroids may be associated with their being in very dilute solutions owing to the difficulty experienced in finding a suitable solvent for them. Following the intravenous injection of oestrogens dilatation of the capillary bed was observed in 8 patients who were either immediately premenstrual, menstruating or had been surgically castrated. In 6 patients where no change was observed they were all in the interval phase of the menstrual cycle. These findings suggest that the capillary vascular responses may be related to the functional activity of the gonads.

Vasodilatation has been observed in the ears of ovariectomized rabbits by Reynolds (1949) who also quotes from Italian work on the nail bed capillary blood pressure. These workers found that the lowest venous pressure occurred premenstrually at a period of high oestrogen blood level and was probably associated with an increase in the capillary bed. Experiments with progesterone, testosterone and desoxycorticosterone acetate have shown little or no effect upon the capillary bed (Reynolds, 1952). Cortisone given orally in large doses has been shown to produce conjunctival capillary ischaemia (Ostfeld *et al.*, 1957) and in one pregnant patient having regular cortisone therapy for lupus erythematosus I found a markedly increased epinephrine sensitivity well above the normal pregnancy range.

It would thus appear that the steroid hormones do have an effect upon the peripheral vascular bed but the exact part they play remains obscure. Studies of the urinary oestrogen excretion levels during the normal menstrual cycle (Brown, 1955) have demonstrated a peak followed by a sharp fall, at midcycle and immediately prior to menstruation. Smith and Smith (1934) have postulated a deficiency of blood oestrogen and progesterone in pregnancy toxaemia and recently Kellar *et al.* (1959) have suggested that there may be a "fall-off" in oestrogen excretion in late pregnancy and in pregnancy toxaemia.

Perhaps the changes that occur in the peripheral vascular bed during menstruation and pregnancy are in some way associated with a lowered production of oestrogen? As oestrogens appear to increase capillary dilatation do they perhaps inhibit the activity of physiological pressor agents? The effect of placental implants for the relief of symptoms in peripheral vascular disease has been ascribed to hormones in the placenta, possibly oestrogens since ethinyl oestradiol also appeared to have some beneficial action (Falconer and Gunn, 1959). Toxaemia of pregnancy is now accepted as being associated with a generalized increase in peripheral resistance and with a disturbed placental physiology. Further studies of the effects on the peripheral vascular bed of placental hormones may help in solving this enigma of medicine.

Summary

(1) Biomicroscopy was utilized to study the bulbar conjunctival vascular bed.

(2) Instillation of a solution of oestrone into the conjunctiva was followed by slight vasodilatation of the capillary bed in 18 subjects.

(3) Instillation of a solution of prednisolone into the conjunctiva was followed by slight vasoconstriction of the capillary bed in 12 out of 38 subjects.

(4) Intravenous injection of an oestrogen preparation was followed by slight vasodilatation of the capillary bed in 9 out of 16 patients.

(5) In 11 patients given an intramuscular injection of a progesterone preparation slight vasoconstriction was observed in the capillary bed in 4 and vasodilatation in one.

Acknowledgments

I am greatly indebted to Dr. William F. Mengert for permission to study the patients under his care and for his advice in preparing this paper.

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FAMILIAL ECLAMPSIA

BY

JOHN C. BROCKLEHURST, M.D., F.R.F.P.S.*

AND

RUTH ROSS, S.R.N., S.C.M.

From the Grenfell Mission, Labrador and North Newfoundland

THIS paper is concerned with ten women who are known to have had fits occurring during pregnancy at the time of delivery. In five cases the fits are known to have been associated with one or more of the following findings—oedema, hypertension (140/90 mm. of mercury, or more) or albuminuria—and were diagnosed as eclampsia by the doctor or nurse who attended them. One woman (No. 6) was seen by the nurse after death and was found to have had fits, oedema, and stillbirth of a 28–32 week baby. The remaining cases (Nos. 1, 2, 3 and 4) have been described by relatives as having had fits with their first two deliveries, in each case one of the pregnancies ending in stillbirth, and in one case in maternal death also.

It seems reasonable to presume therefore that six of these women had eclampsia, and that the other four—although never seen—almost certainly had eclampsia also.

Eight of these women are blood relatives, belonging to different generations of the same family. The two other cases (Nos. 9 and 10) do not belong to this family. They are included because they are directly related to the husband of one of the above women, and to each other.

The women all live within a few miles of each other in the Flower's Cove district of the northern peninsula of Newfoundland. Their forbears came from the United Kingdom about a hundred years ago, to settle in this remote part of the world. They and their descendants have never moved away from this area, and as the population is sparse there has been a good deal of inter-marriage. The people from this area have always been fishermen.

Our attention was focussed on these families when we were concerned with the medical and nursing care of people in this area in the years 1955–57. It seemed that an unduly large number of cases of eclampsia and pre-eclampsia were present among a small proportion of the families in the area, and for this reason it was decided to investigate the family histories of these cases. It was found that the incidence of pre-eclampsia mirrored that of eclampsia presented here. Because of the present equivocation in the status and diagnostic criteria of pre-eclampsia, only the cases of eclampsia are reported.

The family tree of Family "A" which contains the husband or wife of the first 8 cases is presented in Figure 1. This has been pruned to show only the branches in which a case of eclampsia has occurred. Thus although only 5 members of the first generation of family "A" are shown (1, 2, α, β and γ), there were in fact 12 children in this generation. Those that are not shown did not themselves (or their wives) develop eclampsia, nor did any of their descendants.

Similarly, Case No. 1 had 9 pregnancies. Only the 6 which at the time, or in a subsequent generation, were involved in eclampsia are

* Present address: Christchurch Hospital, Christchurch, Hants.

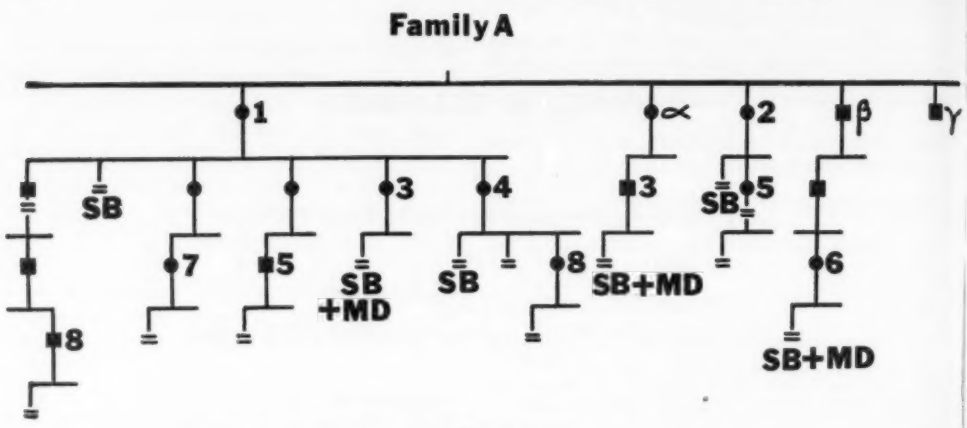

FIG. 1

● = Female. ■ = Male. = = Eclampsia. S.B. = Stillbirth. M.D. = Maternal death.

shown. This then applies to all the branches, and so the figures are very simplified representations of the family trees.

The total number of pregnancies known in family "A"—from the original parents to the latest pregnancy in 1956—is 405. Of these only 31 are represented in Figure 1.

Figure 1 shows all cases of eclampsia known in family "A" (that is 11 cases extending over 4 generations). This gives an incidence of known eclampsia of just under 3 per cent. It is possible that other cases have occurred that have not been described to us.

In an isolated area of this kind it is not difficult to get a complete record of marriages and pregnancies within a family, going back four generations, as is shown here. Information was obtained from several relatives, who were able to give in detail almost the whole history of the family through this period of time. Further, information obtained at different times and places from different relatives showed an almost complete unanimity (except in the order in time of the pregnancies in the earlier generations). Inevitably a number of members of the family have left the district, usually as the result of marriage to an incomer.

Five members of the first generation of family "A" married five members of another family called family "B" (Fig. 2). Of these five marriages, one (γ in the figures) was barren. The other four represent four branches which include all of cases 1–8. It will thus be appreciated that the children of 1, 2, α and β are related to each other not only as cousins, but in fact as both paternal and maternal cousins. The degree of consanguinity is further increased in the second generation by direct cousin marriages in Cases No. 3 and 5, and in the third generation in Case No. 8. Each of these three marriages resulted immediately in a pregnancy with eclampsia.

Figure 1 shows in addition that 7 of the cases in family "A" can trace their inheritance to the original parents of family "A" directly through the female line. Only in Case No. 6 can this not be done. In this case (No. 6) unfortunately the

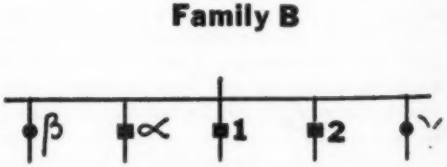

FIG. 2

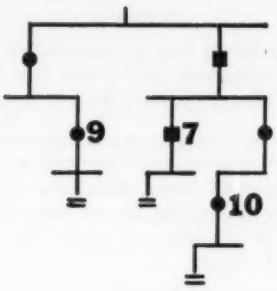

FIG. 3

wife's family could not be traced back beyond her mother, who was not known to have had eclampsia.

It is notable that in this series of 8 cases eclampsia occurred in every case in the first pregnancy. This pregnancy ended in maternal death in two cases (Nos. 3 and 6). In 3 cases there was eclampsia with the second pregnancy as well.

Figure 3 is presented since it shows the relationship of the husband in Case No. 7 to two other cases of eclampsia occurring in his paternal cousin and in his niece. No direct relationship is known between these other cases (9 and 10) and families "A" or "B", and there is no reason to suspect any relationship. Nevertheless they show another example of a familial evidence of eclampsia in this district, although this is by no means so remarkable as in the other cases.

Apart from the cases here described, only one other case of eclampsia is known to have occurred in this area (with a population of under 2,000) in the ten years 1947–56. The family history of this case has been investigated, but is only available incompletely, over the last two generations. In a total number of 147 pregnancies reported in this history, no other case of eclampsia or fits in pregnancy is known.

These cases come from an area where winters are long, cold and dry, summers short, hot and dry. Since the last war there has been little malnutrition in this area, but previously malnutrition was not uncommon. Fertility is high.

Antenatal care has been gradually increasing over the past 20 years, and during the last 10 years it is likely that most pregnant women were seen by a nurse at least once during their pregnancy. Many cases of pre-eclampsia are diagnosed and a proportion of these admitted to the nursing station for delivery.

There seems to be no doubt, comparing the incidence of eclampsia in this family with that of the rest of the population in the area, that there is an exceptionally high incidence in the family here presented.

Unfortunately there has not been an opportunity to study associated factors in this family. A survey of the incidence of essential hypertension and of the cause of death in members of the family in general would be of the greatest value.

DISCUSSION

Much evidence has been presented in the literature to suggest that a tendency to hypertension is inherited. For example, Hines (1937), who applied the cold pressor test to 256 members of 30 families, found that when one parent was either a hypertensive, or a hyper-reactor to this test, 43 per cent of the children were hyper-reactors, while, if both parents showed either of these factors, 95 per cent of the children were hyper-reactors.

Platt (1947) found that 76 per cent of cases of essential hypertension gave a family history suggesting hypertension. Morrison and Morris (1959) conclude that essential hypertension is a specific disease entity which appears to be strongly hereditary.

The whole subject is well reviewed in a leading article in the *Lancet* (1959).

It is generally believed that women who inherit a hypertensive tendency are more likely to have toxaemia during pregnancy. Carey (1959) suggests that such women have inherited a vascular system which is less versatile than normal and cannot adjust so readily to the added demands of pregnancy, and that this contributes to placental insufficiency. On the other hand Barnes and Browne (1945)—from a study of blood pressure readings of 226 relatives of 126 patients in hospital with eclampsia, pre-eclampsia, essential hypertension in pregnancy

and unclassifiable toxaemia together with controls—found no evidence that an inherited tendency to hypertension was of any general importance in the aetiology of toxaemia of pregnancy, other than in cases of essential hypertension in pregnancy.

Platt *et al.* (1958) suggested that an inherited cause of toxaemia in pregnancy might lie in a genetically-based antigenic incompatibility between mother and foetus, but were not able to produce evidence which supported this hypothesis. Pike and Dickins (1954) found a significant increase in group O blood among toxaemic women; but in a later survey (Dickins *et al.*, 1956) they reversed these findings and concluded there was no significant group O preponderance in toxaemia.

Apart from a familial co-incidence of hypertensive phenomena and toxaemia, there have been few reports of familial incidence of eclampsia itself. Bickenbach (1939) reported that 4 out of 39 eclamptic patients had one, two or more cases of eclampsia in the same family. Dieckmann (1952) reports that Anders in a study of 29 cases of eclampsia found an inherited relationship to 4 cases of eclampsia and 6 of pre-eclampsia, but does not state what this relationship is. Malpas (1938) and Neuermann (quoted by Dieckmann) have found a number of eclamptic women with sisters who have had toxaemia.

Whatever may be the inherited basis of eclampsia and fits in pregnancy in the family reported here, there seems little doubt that some inherited factor is present. It is perhaps particularly significant that a direct transmission through the female line can be shown in 7 of these women, and that this cannot be disproved in the eighth.

Summary

(1) The family tree is presented of 4 women who had eclampsia and 4 who had fits at the time of delivery (presumed to be eclampsia).

(2) In the first generation four members of this family married four members of one other family. One of these marriages was barren. The other 3 resulted in—at once or in subsequent generations—11 cases of eclampsia among 8 women.

(3) Seven of these eight women can trace their inheritance back to one original pair of parents directly through the female line. In addition, 3 of them also contracted cousin marriages within the family.

(4) In the case of one of these 7 women, another family tree is presented showing that her husband is also a blood relative of 2 other women who had eclampsia.

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THE BIRTH WEIGHTS OF YORUBA BABIES

BY

DAVID MORLEY, M.D., D.C.H.*
Wesley Guild Hospital, Ilesha, Western Nigeria

AND

GEORGE KNOX, M.D., M.R.C.P., F.S.S.
Department of Child Health, University of Durham, at King's College, Newcastle upon Tyne

AT the present time, there are no fully satisfactory birth weight standards for Nigerian babies. Watt (1959) has published figures for babies in Lagos but he did not separate multiple births nor, in his mixed population, are his figures identifiable with any particular racial group. Furthermore, urbanized populations are exceptional in Nigeria at the present time so the valid application of his results is very limited. The present study is intended to repair the deficiency for West Nigerian rural and semi-rural areas and is confined to a single important racial group, the Yorubas.

MATERIAL

The data consist of the birth weights recorded to the nearest ounce of infants born at the Wesley Guild Hospital, Ilesha, in the years 1940 to 1945, from May to December, 1951, and from October, 1955 to December, 1957, a total of almost nine years. These times were chosen because their records are believed to be complete. Weighing was carried out on the same scales throughout the period, and the scales were under the supervision of a European-trained nursing sister. The infants were normally weighed within two hours of birth, at the time of their first baths.

There were 2,973 deliveries in these periods. Besides birth weight, month and year of delivery, the data included a record of plurality, parity, survival, and whether the admission was booked or an emergency.

The sample was not evenly distributed over the years from which it was drawn, the period from October, 1955 having a much greater number of cases, proportionately, than any other. The overall seasonal distribution was also asymmetrical as a result of the inclusion of part years.

SELECTIVE FACTORS

Hospital data are inevitably selected and if they are to be extrapolated to the general population, some idea of the nature and effects of the selection is needed. Basic population data of frequency of twinning, parity, and so on, are not available in rural Nigeria, and so the nature and extent of selection cannot be stated quantitatively, but only in general terms.

Ilesha is situated (7° 39′ N., 4° 38′ E.) in the rain forest belt of Nigeria. The hospital was built in 1920 and draws its patients from the country town of Ilesha and the surrounding villages. The town has a population of about 80,000, mostly Yorubas, and a population of similar size lives in the surrounding villages. There are probably 6,000 deliveries a year in the area; of these about 1,000 take place in hospital, and about 200 in small maternity homes, these being staffed by midwives with minimum qualifications. The remaining deliveries take place in the patients' homes, on

* Dr. Morley is assisted by a grant from the West African Council for Medical Research.

their farms, or occasionally on the paths in the "bush"; the mother usually delivers with an older female relative, or sometimes with the husband present; not infrequently she manages the delivery by herself. Since only a small proportion of all deliveries takes place in hospital we must ask to what extent they are selected through abnormal pregnancy and delivery. The 2,973 deliveries consisted of 2,118 booked and 855 (28·8 per cent) emergency cases.

The terms "booked" and "emergency" have a rather different meaning in this hospital compared with hospitals in England. In the early 1920s, when maternity work was first started in this area, the local women were loath to give up their traditional methods of delivery in their own homes. The mothers were willing to come for antenatal examination even when they were unwilling to come for delivery. All those attending the antenatal clinics were encouraged to come for delivery and over the following years there has been a steady rise in the number of hospital confinements. But economic and transport difficulties, as well as prejudice, prevent many from attending for delivery and even now less than half of those attending the antenatal clinic present themselves for delivery. All who do so are accepted. The term "booked" is restricted to those who have attended the antenatal clinic on at least two occasions; all the remainder are classed as emergency deliveries. In these circumstances we think it fair to regard booked deliveries as not selected directly in terms of abnormal pregnancy. It is possible that the duration of labour, itself possibly correlated with birth weight, could have biassed our results, but it does not seem likely that the effect of this could be very great except through its relationship with birth rank. We were also able to demonstrate that the birth weight distributions of emergency and booked deliveries were essentially similar, and so have regarded the total group of births as largely unbiassed in any direct manner.

However, there is certainly a good deal of indirect bias in our sample. Some of it is demonstrable as we shall show in respect of birth rank, but much may only be surmised. For example, since social prejudices prevent mothers from coming into hospital it is probable that our sample represents disproportionately the more socially advanced sections of the population and in terms of birth weights may result in an over-estimate.

Of 2,908 deliveries in which the number of previous children was reported, 1,101 (37·9 per cent) were in primiparae. We know that the population proportion of primiparous births must be very much less than this figure. For example, at Imesi, a village near Ilesha, a longitudinal study of infants from prenatal life till the fifth birthday is being carried out, and 500 consecutive parturient mothers in the village have been questioned. Only 62, or 12·4 per cent, were primiparae.

Over the years under consideration, this selection with regard to parity has changed for a variety of reasons and as the number of deliveries in the hospital increased, the proportion of multiparous women also increased. In the years of the survey the successive percentages of the multiparous women were: 43, 54, 44, 35, 43, 53, 71, 60, 66, 66.

As we shall show, selection by birth rank is likely to bias birth weights and this must be allowed for when extrapolating. It is also likely to affect the apparent incidence of multiple pregnancy and the population figure may be different from the 5·3 per cent observed in the sample. Partly for this reason, we shall present the birth weight data for twins and singletons separately.

Observed Birth Weight Distributions

(a) *Singletons*

The birth weight distribution of 2,806 babies in which the weight was accurately recorded is given in Appendix I. The mean birth weight was 6·17 pounds (6 pounds 3 ounces; 2·801 kg.) and percentiles* are given in Table I. These are

* Percentiles are a convenient method of expressing together the centre-point, the width, and the shape of a distribution. The "n"th percentile is the measurement below which n per cent (and above which 100-n per cent) of the observations occurred. An individual measurement may be compared with a percentile scale and an expression obtained of the extent to which it is unusual or abnormal.

TABLE I

Percentiles of Birth Weights in Pounds and Ounces of Yoruba, Compared with South African Singleton Babies

	Percentiles								
	1	5	10	25	50	75	90	95	99
Yoruba (Nigeria)	3–2	4–6	4–15	5–10	6–4	6–13	7–6	7–12	8–10
Indian (South Africa)*	3–5	4–5	5–1	5–12	6–8	7–3	7–12	8–5	9–6
Bantu (South Africa)*	3–9	4–10	5–3	6–2	6–13	7–7	8–4	8–8	9–7
Coloured (South Africa)* ..	3–5	4–15	5–8	6–2	6–13	7–9	8–5	8–13	9–13
European	4–11	5–9	6–1	6–12	7–8	8–4	8–14	9–6	10–2

* These figures for South African birthweights are taken from Salber, E. J., and Bradshaw, E. S. (1951).

compared with birth weight distributions of several racial groups in South Africa; the percentiles have been worked out from birth weight distributions given by Salber and Bradshaw (1951).

(b) *Twins*

The full distribution of the 309 twins in whom the birth weight was exactly recorded is given in Appendix II. The mean birth weight was 4·57 pounds (4 pounds 9 ounces; 2·073 kg.). The percentiles are given in Table II.

TABLE II

Percentiles of Birth Weights in Pounds and Ounces of Yoruba Twins

Percentiles						
5	10	25	50	75	90	95
2–8	3–4	4–0	4–9	5–3	5–15	6–8

FACTORS AFFECTING BIRTH WEIGHT

(a) *Parity*

As is well known in European populations, parity had a well-marked effect upon birth weight. The distribution at different birth ranks is given for singletons in Appendix III. The mean weights at successive ranks are given in Table III. The mean weight rises with rank, and by more than half a pound between first and second babies.

TABLE III

Mean Birth Weights (Pounds) of Yoruba Singletons by Birth Rank

	Birth Rank				Total
	1	2	3	4 or More	
Mean Weight	5·8	6·4	6·5	6·6	6·2

(b) *Season and Year of Birth*

We examined the possibility that improving nutritional standards might have caused an increase in mean birth weight over the period reviewed and found, for singletons, an increase from 6·19 pounds in the period 1940–1945, to 6·31 pounds in the period 1951–1957. However, we attribute this entirely to an increasing proportion of multiparous births in the hospital sample. When primiparous births are examined alone there is no evidence of an increase; the mean weights, here, in the two periods were 5·91 and 5·74 pounds. Furthermore, analyses of diets of pregnant women have shown that they are still so grossly deficient in protein that there could scarcely have been any real improvement.

Both malarial infestation and the availability of foodstuffs have seasonal variations and the former is known to affect birth weight (Cannon, 1958), so we examined the possibility of a seasonal variation in the mean weight. There was

no evidence of it in the total group of singletons. However, we did find some evidence of this in the primiparous women (who have the smallest babies and the highest incidence of placental malaria). Asymmetry was maximized by dividing the year into the two six-month periods May–October and November–April; the mean birth weight in the first period was 5·740 pounds and in the second period 5·836 pounds. The difference was 0·096 pounds, or 1·5 ounces. (See Appendix IV.) This difference did not, in fact, reach that required for formal significance at the 5 per cent level ($F=3·17$ against the required 3·84), but in May–August the mean weight was 2·6 ounces less than in the remainder of the year and this is statistically significant ($F=5·6$ $P<0·025$). The lack of prior justification for using this arbitrary division, except in so far as it corresponds roughly with the wet and dry periods of the year, detracts from the reliability of the result and we would not rely upon this finding alone. However, we shall present data in a subsequent paper which tends to establish its reality.

Discussion

There are many serious difficulties in collecting simple data such as we present, in underdeveloped rural areas. We may justify the trouble of collection and presentation partly on the grounds that such data may prove historically unique and that the economic and social circumstances which will eventually permit more refined and systematic studies may also change the results.

The main source of bias in the present sample is probably through selection in favour of primiparous deliveries. We think the proportion of first babies in this sample may be three times that in the general population. If this were so, the mean weight of a more representative sample of singleton births would be about 6·4 pounds instead of the mean value of 6·2 pounds observed in the hospital sample. For extrapolation of our data to the general population, we would have to correct for this and this might raise all the percentile values by about three ounces.

Even with this possible bias, it is obvious that the weights of Yoruba newborns are much lower than European babies. It has been recorded before that African babies are smaller than European, but even by African standards the rural Yoruba birth weights are low. In Table I, the birth weights at each percentile are lower than for Bantu babies living in urban conditions in South Africa. The mean weight for Yoruba first-borns must be one of the lowest on record, although Columbine (1950) gives somewhat similar figures for Ceylon. Data for Northern Nigeria given by Gardner and Gardner (1958) would also probably give similar results if analyzed by birth rank since the mean birth weight for their series (6·016 pounds) was almost exactly that of our singleton and twins combined (6·011 pounds).

The reasons for these small weights are not yet understood. They may in part be genetic, or if not genetic otherwise predetermined through nutritional effects upon the size of the mother. But there are other more immediate environmental factors at work, also.

Malarial infection of the placenta is known to be associated with a reduced birth weight (Bruce-Chwatt, 1952; Archibald, 1956). This has been confirmed in Ilesha by Cannon (1958) who showed a difference in weight of 11 ounces between infants born with infected and non-infected placentae. He found that infection was much more common in primiparous women; out of 120 primiparae 75 (62 per cent) had parasites in the placenta, while out of 145 mothers of high parity (4 or more) there were only 20 (14 per cent). The highest parasitaemia rates occur in the earliest months of the rainy season and could well explain a subsequent reduced mean birth weight in the middle of the year.

Cigarette smoking in the mother has been found to be related to a low birth weight in white infants (Simpson, 1957) without being related to the length of gestation or the obvious complications of pregnancy (Lowe, 1959). An unknown but considerable proportion of the women attending the hospital in Ilesha chew locally grown tobacco but as yet we have no data relating to its possible effect in reducing the birth weights of their infants. This we intend to study.

Summary

This is a study of birth weights in 2,973 Yoruba babies born in hospital in a country district of Western Nigeria.

The sample was not biassed in terms of deliberate selection of abnormal pregnancy, but was subject to other forms of bias and, with respect to birth weight, the most important was selection by birth rank. The sample contained three times the proportion of first births compared with the population of the area.

The mean weights and percentiles are given for singletons and twins and a mean weight of 5·8 pounds for Yoruba first-borns is one of the lowest on record.

The reasons for the low weights are not understood but genetic factors, malaria of the placenta, nutritional inadequacy in pregnancy, nutritionally-determined small stature in the mothers, and the effects of tobacco, all merit further study.

There are difficulties in collecting such data as these in underdeveloped rural areas, and other difficulties, particularly with regard to sampling errors, in interpreting them. But such data may be historically unique, biologically illuminating and a first necessity in the planning of definitive modes of health ascertainment and preventive action.

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Appendix I

Weights of Singleton Babies

Pounds	Ounces 0–3	4–7	8–11	12–15
1	1	—	—	—
2	5	3	3	10
3	17	14	21	21
4	30	63	54	65
5	120	160	208	236
6	291	344	293	251
7	212	135	96	60
8	39	20	15	10
9	6	—	1	1

This table contains 2,806 entries consisting of 2,652 survivors, 56 deaths and 98 stillbirths. The remaining 9 infants had their weights recorded with insufficient accuracy for inclusion, or their survival status was not recorded.

Appendix II

Weights of Twins

Pounds	Ounces 0–3	4–7	8–11	12–15
0	—	—	—	4
1	1	—	—	3
2	2	4	4	4
3	7	9	16	16
4	34	25	42	33
5	26	16	20	9
6	12	7	3	7
7	3	1	1	—

This table contains 309 entries. The remaining seven infants were not recorded with sufficient accuracy for inclusion.

APPENDIX III

Birth Weights of Singletons by Birth Rank

	Birth Rank				
	1	2	3	4+	Totals
Pounds:					
0–	—	—	—	1	1
1–	1	—	—	1	2
2–	9	2	5	6	22
3–	43	10	9	10	72
4–	146	18	8	35	207
5–	407	101	68	134	710
6–	363	242	186	364	1,155
7–	98	82	80	228	494
8–	7	16	19	40	82
9–	1	2	1	4	8
Total infants	1,075	473	382	823	2,753
Total weights (pounds) ..	6,233·5	3,019·5	2,479·0	5,400·5	17,132·5
Mean weights (pounds) ..	5·80	6·38	6·49	6·56	6·22

Mean weights of groups are taken as 0·5 pounds greater than the minimum value for inclusion in the group.

APPENDIX IV

Mean Birth Weights by Season in Primiparous Singleton Deliveries

	January	February	March	April	May	June	July	August	September	October	November	December
Mean weight (pounds)	5·84	5·75	5·86	6·00	5·63	5·78	5·78	5·57	5·87	5·80	6·00	5·83
					5·68 against 5·85 in remainder of year							

TWINNING IN YORUBA WOMEN

BY

GEORGE KNOX, M.D., M.R.C.P., F.S.S.

Department of Child Health, University of Durham, at King's College, Newcastle upon Tyne

AND

DAVID MORLEY, M.D., D.C.H.*

Wesley Guild Hospital, Ilesha, Western Nigeria

IN a study of the birth weights of Yoruba babies born in hospital at Ilesha, West Nigeria, we noted (Morley and Knox, 1960) that 159 of 2,973 women, 5·3 per cent, had multiple pregnancies. There was one set of triplets, the remainder being twins, so that 10·1 per cent of all newborn infants were from multiple pregnancies. This was so much greater than the proportion expected in European populations that we decided to examine the matter further and, in particular, to examine those selective factors which might have biassed our estimate of incidence and biological factors which might throw light upon so high a rate of twinning.

The sources of the material have already been described (Morley and Knox, 1960).

SELECTIVE FACTORS

First we considered whether an antenatal diagnosis of suspected twins might have influenced the chances of a hospital delivery in this population. We can say at once that there was no deliberate medical selection, for all cases presenting for antenatal care are encouraged to enter hospital for delivery and none is refused. Only half of all mothers so attending are in fact delivered in hospital. It is possible, of course, that the degree of encouragement applied may vary from case to case and might result in a higher admission rate for twin pregnancies than for singletons, but it is believed that the important determinants of whether or not a woman is admitted to hospital are concerned with social customs, family circumstances, transport and finance, rather than the obstetric diagnosis. It might be suggested further that the emergencies and difficulties associated with twin deliveries might result in a disproportionate number reaching hospital. Again we do not think this is important in this hospital and the twin-rate among "emergency" admissions (6·1 per cent) was only slightly greater than in "booked" admissions (5·0 per cent). Statistically, this is not significant. For these reasons we think it unlikely that selection related directly to the occurrence of a twin pregnancy can have influenced the twinning rate in our sample to any great extent.

But it is certain that important degrees of selection have occurred indirectly, particularly in relation to birth rank. This factor has been shown in other populations to have important effects upon the chances of a twin pregnancy and the same will be shown from our own data.

The hospital population was distributed according to birth rank as shown in Table I; 38 per cent were recorded as primiparous deliveries. This proportion is much closer to the structure of a European population than an African one and there must have been strong selection according to rank. We do not know the exact proportion of primiparous deliveries in the general Nigerian population, but considerations of childhood mortalities and

* Dr. Morley is assisted by a grant from the West African Council for Medical Research.

TABLE I

Twinning Rates by Birth Rank

	Birth Rank							NR.	Total
	1	2	3	4	5	6	7+		
Twin pregnancies	26	22	25	23	22	16	21	3	158
Singleton pregnancies ..	1,075	473	382	284	224	147	168	61	2,814
Total	1,101	495	407	307	246	163	189	64	2,972
Per cent twinning	2·36	4·44	6·14	7·49	8·94	9·82	11·1	—	5·32

population-equilibria would lead us to expect a proportion less than half of that observed in the hospital sample. Furthermore, we have complete data for one of the local villages (Imesi) over a recent period, where only 62 of 500 deliveries, 12·4 per cent, were primiparous.

Since this selection has a social basis it probably operates progressively at successive birth ranks. The twinning rate also rises progressively with birth-rank and it is possible therefore that the population twinning rate could be 50 per cent greater than that observed in the sample.

This is reflected in another variant, namely the year of admission to hospital. In the period 1940–45, 4·5 per cent of maternities were multiple, while in 1956–57, when the proportion of multiparae had risen (Morley and Knox, 1960) 5·9 per cent were twins.

BIOLOGICAL FACTORS

As already stated, we found an increasing twinning rate with rising birth rank (Table I). From 2·4 per cent of first pregnancies, the proportion rose to over 11 per cent of high ranks (7 or more).

The identification of groups with twinning rates over 10 per cent is remarkable by European standards. Waterhouse (1950) examined the Registrar General's data for England and Wales between 1938 and 1948 and found an overall twinning rate of 1·2 per cent. Among birth ranks of 7 or higher, the English figure is 1·8 per cent, less than a sixth of the comparable Nigerian rate. The Nigerian figure, even for first births, is considerably greater than the highest figure for any single age-parity group in the English data. The effect of rank seems also to be steeper in Nigeria than in England; in Nigeria the highest ranks have more than four times the twinning rate of first pregnancies, while in England the factor is less than two.

It is not only by European standards that this twinning rate is unusually high for we have not found any record of a higher one. The only approximation to our rates was recorded by Columbine (1950) in a maternity hospital in Colombo, Ceylon. His data give the following percentage twinning rates compared with our own:

	Birth Rank		
	1 and 2	3 and 4	5 and later
Colombo ..	2·3%	4·7%	6·5%
Ilesha ..	3·0%	7·2%	10·9%

This was of particular interest because Columbine's data resembled our own in supplying also a close approach to the very low mean birth weight for Yoruba singletons, and the double likeness in the two sets of data suggests that there may be common biological determinants for both phenomena.

Because the most obvious biological differences between African and European reproduction are related to malnutrition and malarial infection and both have seasonal cycles, it was interesting to find evidence of a seasonal variation in the twinning rate. The relevant data are set out in Table II. The monthly frequencies

TABLE II

Twinning by Month of Birth

	January	February	March	April	May	June	July	August	September	October	November	December	NR.	Total
Twin pregnancies ..	6	12	9	10	17	11	17	17	15	19	14	11	—	158
Singleton pregnancies ..	196	191	196	218	124	208	153	199	247	290	321	281	—	2,814
Total	202	203	205	228	231	219	270	216	262	309	335	292	—	2,972
Per cent twinning ..	2·97	5·91	4·39	4·39	7·36	5·03	6·30	7·87	5·73	6·15	4·18	3·77		

from May to October are all over 5 per cent, and all but one of the others are below this level. The difference between these two half years is statistically significant ($\chi^2=6{\cdot}33$, $P<0{\cdot}025$) to a degree which goes some way to compensate for the arbitrariness of the dichotomy. (For example, it is still significant if taken as possessing two degrees of freedom.)

Moreover, we found that there was actually an inverse correlation between mean monthly birth weights (Morley and Knox, 1960) and twinning rates. Spearman's Rank Correlation Coefficient gave the highly significant value of $-0{\cdot}769$. This reinforces the suggestion we made in comparing our results with Collumbine's (1950) data, that twinning rates and low birth weights may share common biological causes. It is possible of course and even likely, that the common biological determinants of the two phenomena are out of phase by one year: that is, the determinants of one year's seasonal fall in birth weights are correlated with those of the next year's seasonal rise in twinning-rate.

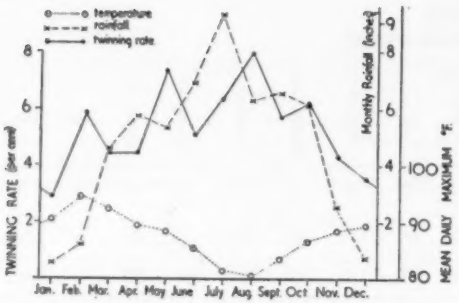
Ilesha is situated in the Tropics (7° 39′ N., 4° 38′ E.) and seasonal variations are more difficult to interpret than in regions where the annual variation of solar declination is monophasic. But in fact, the important meteorological indices for the district each show only one clear cycle in the year, as shown in Table III and

TABLE III

*Seasonal Meteorological Data**

	January	February	March	April	May	June	July	August	September	October	November	December
Monthly rainfall (inches)	0·45	1·19	5·28	5·77	5·23	6·81	9·31	6·23	6·30	6·02	2·43	0·37
Monthly mean daily temperature ° F.:												
Maximum ..	90·7	94·0	92·4	89·7	88·5	85·6	81·7	80·5	83·3	86·3	88·1	89·5
Minimum ..	66·0	65·5	72·3	72·1	71·2	70·2	69·3	68·3	69·8	69·8	68·9	67·9

* Computed as the means of four readings: at Oshogbo Aerodrome in 1957 and 1958, and at Oshogbo-Ede Waterworks in 1956 and 1957. Oshogbo is 20 miles from Ilesha.



The incidence of twinning in Yoruba women in relation to seasonal variations of rainfall and temperature

FIG. 1

Figure 1. It can also be shown that the twinning rate has statistically significant correlations with these cycles at certain orientations. For example, the Spearman Rank Correlation Coefficient between the twinning rate and the mean maximum daily temperature for the fifth month before delivery is +0·755, and for rainfall 11 months before delivery it is +0·692; both are statistically significant. Direct inferences concerning mechanisms may not be drawn from this and the reliability of the correlations is modified by the arbitrariness of the orientations needed to produce them. The correlations do not reinforce further the evidence already presented for the statistical significance of a cycle but add to the validity of supposing that there must be a biological explanation. We examined the possibility of a seasonal variation in the proportion of primiparous deliveries and found no evidence of such an explanation.

Finally, our data supply some information regarding zygosity. We knew the sex constitution of 149 pairs, the distribution being MM, 39; MF, 68; FF, 42. Using Weinberg's simple method of subtracting unlike from like, we have an estimate of 13 pairs of monozygotic twins. It appears that the great majority of twins in this population, about 91 per cent, are dizygotic. This is entirely in accord with other observations (for example, Waterhouse, 1950) that it is dizygotic twinning in particular whose frequency is related to maternal age.

SUMMARY

In a study of Yoruba mothers living in a rural area of Western Nigeria and delivered in hospital the incidence of twin pregnancy was 5·3 per cent. This is the highest figure we can find for any community in any part of the world.

What is more, a high proportion of primiparae in this sample compared with the local population as a whole makes it almost certain that this is an under-estimate.

The incidence of twinning rose with birth rank and there appeared to be a seasonal cycle. The great majority of twins (91 per cent) were dizygotic.

There is evidence to suggest that the high twinning rates and the low birth weights of singletons in this community are in some way causally related.

ACKNOWLEDGMENT

We wish to thank the Director of the Ministry of Communications and Aviation Meteorological Division for climatic data.

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ANAEROBIC COCCI IN THE VAGINA OF NATIVE WOMEN IN BRITISH NORTH BORNEO

BY

RONALD HARE, M.D.

AND

IVAN POLUNIN, D.M., M.A., B.Sc.

From the Department of Bacteriology, St. Thomas's Hospital Medical School, London, and the Department of Social Medicine and Public Health, University of Malaya in Singapore

IN a previous paper (Polunin, 1958) the suggestion was made that de-population amongst the Muruts, a tribe living in the interior of British North Borneo, was largely due to failure to bear children, it having been found that as many as 40 per cent of Murut women who had ever been married had not had a living child. The explanation advanced for this sterility was that it was largely due to gynaecological abnormalities such as thickening or distension of the Fallopian tubes of such a character as to prevent conception by blocking their lumen, or alternatively, retroversion of the uterus due to adhesions which would lead to abortion if conception were to occur. Examination of a series of 27 Murut women complaining of infertility showed that no less than 20 (74 per cent) had lesions of this description and somewhat similar findings were obtained in a study of another 41 women from neighbouring groups where sterility was a serious problem.

It is probable that these lesions are not the sequelae of gonorrhoea but that they result from post-abortal or post-partum infection. Little is still known of the organisms likely to cause pathological changes of this description following abortion, but the more severe forms of post-partum infection are generally due to either *Streptococcus pyogenes* or anaerobic cocci (Schwartz and Dieckmann, 1927; Schottmuller, 1928; Colebrook, 1930; Douglas and Davis, 1946; Hill, 1950). The latter are almost as important as the former for, in an investigation of 384 cases in London in 1931–33, anaerobic cocci were almost certainly the cause of infection in 157 and *Strep. pyogenes* in 208 (Rivett *et al.*, 1933).

Of the two organisms, anaerobic cocci are more likely to produce the lesions observed in Murut women because they tend to produce abscesses in the broad ligaments or Fallopian tubes and thrombosis of the pelvic veins with suppuration of the surrounding connective tissues (Colebrook, 1930; Colebrook and Hare, 1933; Rivett *et al.*, 1933). Such lesions might well result in the formation of so much scar tissue as to lead to infertility. Furthermore, these organisms are common inhabitants of the birth canal, between 20 and 40 per cent of women having them in the vagina during pregnancy (Soule and Brown, 1932; White, 1933; Thomas and Hare, 1954), and there can be no doubt that in many cases of infection they have been inoculated on to the placental site as a result of intra-uterine manipulation during or after delivery (Colebrook, 1930; Colebrook and Hare, 1933; Rivett *et al.*, 1933).

Streptococcus pyogenes, on the other hand, seldom produces localized pelvic inflammation, generalized peritonitis or bacteraemia being more usual. There is also little doubt that nearly all uterine infections by this organism are due to its transfer from the nasopharynx of an

attendant during delivery (Smith, 1931, 1933; Colebrook, 1935; Paine, 1935; Courmont and Sédallian, 1931); it therefore follows that it must be capable of surviving in nasopharyngeal carriers in communities like the Muruts that are unusually small and isolated. From what is known of this organism, such continuous survival over a period of many years would be unlikely.

If the pathological changes observed in Murut women are the end results of infection by anaerobic cocci, the only satisfactory proof of this would necessitate bacteriological examination of cases as they occur. This is out of the question at the moment because the population is sparse and inaccessible, but it appeared worthwhile to ascertain, firstly, whether anaerobic cocci occur in the vagina of women in remote tribes, secondly, whether any that are found resemble those responsible for the severe infections in other countries, and thirdly, whether higher vaginal carrier rates are found in "infertile" populations (i.e., populations where infertility is a serious problem) than in "fertile" populations living in the same area.

The opportunity to do this came in December/January, 1958/59 when one of us (I.P.) went to North Borneo, a preliminary account of this work being given in Polunin (1959). Vaginal swabs were taken from an "infertile" group of 46 Muruts and 14 from neighbouring tribes and a "fertile" group of 37 Dusuns who do not suffer from infertility.

Methods

Media. Screw-capped bottles (1 ounce capacity) with a rubber diaphragm were three-quarters filled with Robertson's meat medium. The bottles were then filled as completely as possible with liquid paraffin, sterilized by autoclaving and taken into the field. Before use, as much as possible of the remaining air was driven out by inserting a sterile intradermal needle through the diaphragm and standing the bottle upright and up to the neck in boiling water for at least 15 minutes. The needles were then removed and the bottles allowed to cool.

Specimen taking. The woman was placed in the left lateral position and the cervix visualized using a duckbill or Sims speculum. A cotton wool swab on a bamboo stick (previously sterilized by autoclaving) was employed to obtain mucus from the cervical canal and immediately thrust into the Robertson's medium prepared as above. The swab was then cut short with sterile bone forceps and the stopper screwed tight.

Incubation and Transport. No incubator was available, but the bottles were left at room temperature, which varied from 65°–90° F., for 24–30 hours, the longer period being employed in the hills where the temperature was lower. The bottles were then kept in a refrigerator or in a vacuum flask packed in ice until a batch could be sent, similarly packed, to Singapore.

Freeze drying and transport to London. About 0·25 c.cm. of the fluid portion of each culture was mixed with an equal volume of ox serum, freeze dried in an Edwards spin drier, the tube sealed off under vacuum, and sent by air to London.

Labelling. The specimen from each patient was given a number at the time it was taken. It was not until the specimens had all been processed and the differentiations almost over that the source of each specimen was divulged to the London observer (R.H.), so that personal bias was minimized.

Isolation in London. On receipt the tubes were kept in the refrigerator until they could be processed. A suspension of the contents was made in broth and horse blood agar plates were inoculated and incubated anaerobically in a McIntosh and Fildes jar for 48 hours. Using a hand lens, specimens of each type of colony were then picked, and purified by repeated plating if necessary. Two blood agar plates were then inoculated in parallel from single colonies and one plate was incubated aerobically and the other anaerobically. If no growth occurred on the former, and the organism was a coccus, tubes of Robertson's meat medium sealed with vaseline were inoculated and incubated for 48 hours for preservation. In this way several colonies were frequently isolated from each individual. Differentiation of the anaerobic cocci was carried out by the method of Thomas and Hare (1954).

TABLE I

Anaerobic Cocci Isolated from High Vaginal Swabs Taken from Women in North Borneo

Population	Number Sampled	Number with Anaerobic Cocci	Percentage Carriers of Anaerobic Cocci	Number with Representatives of Two or More Groups	Number of Strains Classified	Classification of the Strains							
						Group							Not Grouped
						I	II	III	IV	VI		IX	
										a	b		
"Infertile" not pregnant	47	20	42·6 } 38·3	7	28	18	1	1	1	2	2	2	1
"Infertile" pregnant ..	13	3	23·0 }	0	3	2	0	0	0	0	0	1	0
"Fertile" pregnant ..	24	3	12·5 } 10·8	0	3	0	0	0	0	0	2	0	1
"Fertile" not pregnant ..	13	1	7·7 }	0	1	1	0	0	0	0	0	0	0

RESULTS

Of the 60 specimens obtained from the "infertile" population, 47 were from women who were not pregnant and were complaining of infertility, the remaining 13 being from pregnant women in the same communities.

No difficulty whatever was encountered in isolating anaerobic cocci from the specimens. Indeed in many instances they were the only organisms present. As will be seen from Table I anaerobic cocci were isolated from 20 of those who were not pregnant and from 3 of those who were pregnant giving carrier rates of 42·6 per cent and 23·0 per cent respectively.

Much lower carrier rates were obtained from the "fertile" populations. Three out of 24 (12·5 per cent) who were pregnant and one out of 13 (7·7 per cent) of those not pregnant had anaerobic cocci.

Study of the strains isolated showed that the great majority were members of Group I and identical in behaviour with those previously studied by Hare *et al.* (1952) and Thomas and Hare (1954). Representatives of Groups II, III, IV, VI and IX were also found but much less often. As in previous investigations, members of two or even three Groups were occasionally isolated from one specimen.

DISCUSSION

Although specimens were obtained from women from "infertile" and "fertile" populations and anaerobic cocci were found much more often in the former than in the latter, it must be emphasized that the two groups are not strictly comparable. The majority of the specimens from the "infertile" population came from non-pregnant women whereas most of those from the "fertile" population were pregnant.

With regard to the latter, the carrier rate 12·5 per cent was undoubtedly very much lower than that obtained in several investigations on pregnant women in other countries; Soule and Brown (1932), for example, found that 39·5 per cent of 207 American women were carriers. In similar examinations in London, White (1933) obtained a carrier rate of 33 per cent and Thomas and Hare (1954) found 23·7 per cent. In all three investigations, however, the specimens were examined at once and colonies could be picked from solid media for identification, whereas in the present investigation the primary cultures were made in Robertson's meat broth. This suffers from the obvious disadvantage that small numbers of slow growing organisms may be overgrown by other species. This may explain the low carrier rate amongst those who were pregnant in the fertile population.

If this be so, the high carrier rate of 42·6 per cent amongst the "infertile" non-pregnant population acquires an added significance for the true carrier rate may be very much higher. Nevertheless, a high carrier rate may also be usual in non-pregnant women as Rosowsky (1912) found that 40 per cent of 65 women and 15 children carried anaerobic cocci in the vagina. But this seems to have been the only investigation so far reported on non-pregnant women.

Whatever may be the real significance of the low carrier rate amongst the fertile and the high carrier rate in the infertile population, there is

no doubt that anaerobic cocci belonging to Groups I, II, III, IV, VI and IX are present in the birth canal of women in the interior of North Borneo. In this respect they resemble women in England because Thomas and Hare (1954) isolated the same groups from high vaginal swabs taken during pregnancy. But unlike the women studied by Thomas and Hare, the great majority of the strains isolated from Borneo women were members of Group I. Thus the carrier rate for this Group alone was 38·3 per cent in the "infertile" non-pregnant and 15·3 per cent amongst the "infertile" pregnant women, whereas in Thomas and Hare's series of 93 pregnant women, the carrier rate for Group I was only 4·3 per cent and in the "fertile" Borneo population it was 2·7 per cent.

There is much evidence to suggest that the members of Group I are by far the most important causes of anaerobic coccal infection after delivery. Of 60 strains from such infections studied by Thomas and Hare (1954) no less than 42 or 70 per cent belonged to this Group. There are also reasons for supposing that a high proportion of the strains isolated from cases of puerperal infection in the past, before the introduction of antibiotics or the method of classification used in this paper, belonged to this Group. They invariably grow in the form of chains, ferment glucose, maltose and fructose and produce 1–2 c.cm. of gas from 4 c.cm. of medium provided it contains a sulphur compound such as sodium thiosulphate, glycocholate or cystine. Horse serum or blood may even contain sufficient sulphur for this purpose. Galactose is not fermented but some strains act on sucrose sufficiently to depress the pH of the medium from its initial 7·6 to 6·8–7·0. The strains isolated and named *Strep. putridus* by Schottmuller (1930) had many of these characteristics and were shown by him to be responsible for many cases of puerperal fever. There is no doubt that the same organisms were frequently encountered by other workers (Schwartz and Dieckmann, 1927; Harris and Brown, 1929; Colebrook, 1930; Colebrook and Hare, 1933; Rivett *et al.*, 1933). It is thus clear that a very much higher proportion of Murut than English women are vaginal carriers of a variety of anaerobic cocci which can cause severe pelvic inflammation after full-term delivery.

Because many of the Murut women complaining of infertility had never given birth, infection following full-term delivery cannot have been responsible for all cases of infertility. It is however known that abortion—whether induced or not has never been determined—is a common event in these tribes and that it is sometimes followed by infection. Unfortunately, the part played by anaerobic cocci in septic abortion still awaits detailed investigation. There is, for example, no agreement as to the number of cases from whom anaerobic cocci can be isolated, Hill (1950), in Australia, having found them in 60 per cent whereas Ramsay, Brown and Manners (1955) isolated them from only 19 per cent of cases in England.

It is thus clear that, although it has been postulated that post-abortal or post-partum infection is a major cause of Murut infertility, and the investigations reported in this paper show that an organism capable of producing pelvic inflammation is unusually common in the birth canal, it is still to be proved that infection by it is the real cause of Murut infertility.

Summary

(1) Sixty high vaginal swabs were obtained from Murut and Dusun populations in British North Borneo amongst which infertility following pelvic inflammation is common.

(2) Thirty-seven similar specimens were obtained from Dusun populations which are prolific.

(3) Anaerobic cocci of Groups I, II, III, IV, VI and IX were isolated from 38·3 per cent of the "infertile" population and 10·8 per cent of the "fertile".

(4) Carrier rates for Group I were 33·3 per cent amongst the "infertile" population and 2·7 per cent in the "fertile".

Our thanks are due to the Government of British North Borneo, the University of Malaya and Professor T. A. Lloyd Davies. Also to Professor J. H. Hale and the Department of Bacteriology in the University of Malaya for

preparing the media and processing the specimens.

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SUBCHORIAL HAEMATOMA MOLE: HYPOTHETICAL AETIOLOGY

BY

RICHARD TORPIN, M.D.

Chairman

Department of Obstetrics and Gynaecology

Nemazee Hospital, Shiraz Medical School, Red Lion and Sun Hospital, Shiraz, Iran

SUBCHORIAL haematoma mole was first described by Carl Breus (1850–1914). Since then many cases have been presented and probably myriads of others have gone unnoticed.

An examination of most specimens I have seen and of those illustrated in the literature reveals an excessive area of placentation in relation to the area of the membranes and many of these show a ring development (Fig. 1) similar to that observed in a circumvallate placenta. This is so common that it seems that many of them would have eventuated into such a condition had the pregnancy not been terminated by decidual haemorrhage behind the placenta.

This haemorrhage apparently is of such nature as to invade the villous portion from behind and to form haematomas underneath the chorion and of course beneath the amnion. These haematomas have a tendency to obliterate the amniotic cavity by compression. The extensive separation of the placenta occasioned by the haematomas causes death of the embryo which atrophies and, if the products of conception are retained long enough, the embryo becomes a mere nubbin or disappears altogether.

All of these conditions may be most readily explained by a relatively deep implantation of the fertilized ovum into the decidua so that an excessive number of primordial chorionic buds covering the surface of the ovum are able to lie adjacent to vascularized decidual cells. Variation in depth of implantation of the human ovum is proved by the rare occurrence of a lower monkey type of attachment. In such cases the fertilized ovum lies in the practically obliterated uterine cavity and attaches to both anterior and posterior wall.

The wall surrounding the amniotic cavity in the deeper variety is mainly placenta, in the early stages, so that the usual relationship of placental area to membrane area is reversed and the sac may be composed of three-quarters or more of placenta and one-quarter or less of membranes. Such is probably the situation in early placenta circumvallata and most certainly of greater degree in the case of early placenta membranacea. This abnormal relationship of the foetal sac to the uterine wall is similar to the conditions in ectopic pregnancy which is very prone to early retro-placental bleeding.

The hypothesis then is that subchorial haematoma mole, placenta circumvallata and placenta membranacea all arise from excessively deep implantation of the fertilized ovum into the uterine decidua. To allow this deep penetration of the ovum, the decidua may be disordered, probably by some degree of hyperplasia.

Placentation in abortions, in premature separations of the placenta, in placenta praevia and placentation at term have been studied since 1931. Some of the bibliography leading up to this hypothesis is appended.

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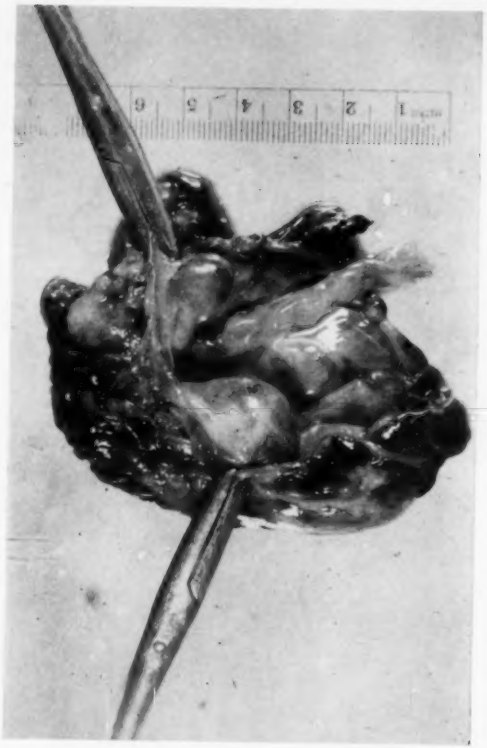

FIG. 1

Breus subchorial haematoma mole showing development of a marginal ring as in placenta circumvallata.

ACCIDENTAL RUPTURE OF THE FEMALE URETHRA

BY

NIGEL GOURLAY, M.B., M.R.C.O.G.

Senior Registrar

Department of Obstetrics and Gynaecology at the North Middlesex Hospital

INJURIES to the vulva as a result of falling astride a hard object such as a chair back, occur quite frequently, and although they may be associated with brisk haemorrhage or the formation of large haematomata, it is unusual for such a domestic accident to cause anything but superficial damage. The injury reported here, followed a fall astride the sharp edge of a kitchen stool which resulted in extensive laceration of the anterior vaginal wall and complete division of the urethra at a point 1½ inches (3·75 cm.) from the external urethral meatus.

Although accidental rupture of the male urethra is well recognized, a search through the surgical and gynaecological textbooks has revealed no mention of the condition in the female. The textbooks of urology also say little or nothing about this condition, and those that do, merely mention that it is known to occur—with little further comment. Winsbury-White (1948) mentions the possibility and dismisses the treatment in one short paragraph. Herman (1938) in his textbook very briefly describes one case from his own experience, and in a standard work on gynaecological urology (Everett, 1947) it is not mentioned at all. Clearly this condition does not come readily to the mind of the urologist, for at a recent meeting of the Section of Urology at the Royal Society of Medicine devoted to urethral injuries, no mention was made of the female urethra, and in another recent paper from a gynaecological source, describing injuries to the female bladder and urethra, accidental urethral damage is not considered (Russell, 1951).

A further search in the literature has revealed no published case of accidental rupture of the female urethra over the past 25 years, although Cooke and Smith (1942) report a case in which partial avulsion of the urethra occurred as a result of a straddle accident.

In view of the apparent rarity of this condition it was thought justifiable to report a case and to comment briefly on its aetiology and treatment.

CASE REPORT

The patient, a parous woman of 38, was admitted to hospital 2½ hours after the accident. She had been standing on a kitchen stool in order to reach up to a high shelf; the stool had canted over and she had fallen astride the edge of it. Brisk bleeding had at once occurred and she had summoned her doctor. On admission, moderate bleeding was still going on, she was pale, sweating and cold, and her systolic blood pressure was 50 mm. of mercury. Examination of the heart, lungs and abdomen revealed no abnormality, and there was no evidence of any other injury. She was taken to the operating theatre and a quick preliminary examination was made without anaesthesia with the patient in the lithotomy position. This revealed lacerations of the anterior vaginal wall, and, as it was clear that quite extensive surgery would be required, a temporary pack was inserted to control the haemorrhage, and the patient was resuscitated by intravenous transfusion of Dextraven and blood.

When her general condition had improved, she was examined under anaesthesia. After clearing away blood clot she was seen to have a transverse laceration of the anterior vaginal wall extending across the midline from the region of one pubic ramus to the other. The urethra had been completely divided at a point 1½ inches (3·75 cm.) from the external urethral meatus, and the distal portion had been avulsed from the vaginal wall and was hanging down, attached to the patient only in the region of the external meatus. The anterior vaginal wall was extensively contused, but the vulva and perineum were only slightly bruised and there was no detectable injury to the pubic arch. The proximal end of the severed urethra was identified with some difficulty in the contused

tissue near the bladder neck and a No. 18 F.G. Foley catheter was threaded *via* the external meatus first through the distal urethra and then into the bladder. A small quantity of clear urine was obtained and it was judged that the urethral rupture had occurred about 1 cm. from the internal urethral meatus. The ends of the divided urethra were approximated over the catheter by four sutures of "O" chromic catgut, and the para-urethral tissue and pubo-vesical fascia then brought together in the midline below the urethra and bladder neck with interrupted sutures of catgut. Lastly, the lacerated anterior vaginal wall was repaired with interrupted sutures and a small pack left in the vagina.

By this time the patient had received three pints of blood and her general condition remained satisfactory. Open drainage of the bladder *via* the Foley catheter was instituted on return to the ward, and a course of prophylactic chemotherapy (penicillin and sulphadimidine) started. The vaginal pack was removed on the following day, and an X-ray of the pelvis then revealed no evidence of bony injury. For the first four post-operative days the patient had a low-grade pyrexia, but her recovery was otherwise uneventful, and on the tenth day, when the catheter was removed, normal micturition was re-established without discomfort or difficulty.

The patient was seen again in the Out-patients' Clinic three months later. She was then free of any micturition symptoms and, in particular, had entirely normal urinary control without stress incontinence. Examination revealed a soundly healed and well-supported anterior vaginal wall.

A year later the patient was again seen. Micturition had remained normal, examination revealed no abnormality, and it was possible to insert a No. 18 F.G. catheter without difficulty or discomfort.

Comment

Damage to the female urethra is usually related to childbirth, surgical trauma or irradiation. Accidental rupture, though quite a frequent occurrence in males, appears to be a rare event in females, although, as in the male, it may follow direct trauma or crushing injuries of the pelvis. The difference in the reported incidence may be explained partly by the anatomical differences in the sexes. The short female urethra, lying for the most part deeply surrounded by soft tissue and protected in front by the symphysis pubis, is likely to be much less vulnerable to a direct blow from below than the male urethra, which lies relatively superficial in the perineum for much of its course. However, the apparent rarity of this condition may also be related to the fact that the end results of urethral trauma are perhaps less catastrophic in the female and have, therefore, received less attention in the literature.

The mechanism of direct injury might be expected to be the same as that in the male, where the bulbous urethra is crushed against the pubic arch by a blow from below—and, in fact, both in the case reported here and the one reported by Cooke and Smith (1942), the injury was caused by falling astride the edge of stool or chair. In the latter case, the urethra was separated from the lacerated anterior vaginal wall for almost its whole length, and, although not actually divided, was avulsed at the level of the external urethral meatus and hung free between a flap of anterior vaginal wall posteriorly and the pubic symphysis in front. In the case reported by Herman (1938) the injury followed a traffic accident, of which no details are given, and on this occasion the urethra was divided "just distal to the internal sphincter" and was not associated with any bony injury. It is likely that the high level of the site of rupture in two of these cases was due to the blow coming from behind as well as below, and thus nipping the urethra against the posterior surface rather than the inferior margin of the symphysis. It is of interest that although the site of rupture in two of these cases must have been perilously close to the bladder neck, no actual bladder damage was demonstrated, and both patients subsequently had complete urinary control.

Treatment

The treatment of an acute condition as unfamiliar as this must of necessity be somewhat impromptu, and in retrospect the advisability or otherwise of providing additional suprapubic bladder drainage gave some cause for anxiety. Drainage *via* an indwelling catheter was decided upon mainly on the grounds that it is accepted practice in reconstructive operations upon the female urethra, such as those described by Grey Ward (1934) and Martius (1936) and later advocated by Shaw (1949) and it may also be employed following excision of urethral diverticula in the female. Clearly, these procedures are not strictly comparable, in that complete division of the urethra has

not occurred, but at least they show that such drainage is not incompatible with healing of the female urethra, or healing of a reconstructed urethra. Both Herman's case and that reported by Cooke and Smith were treated post-operatively by drainage *via* an indwelling catheter and no mention is made of subsequent stricture formation. Winsbury-White dismisses the treatment of injury to the female urethra from external violence in one short paragraph. He advocates "only very short periods of indwelling catheter drainage" and adds that suprapubic drainage "may be necessary in bad cases of injury".

In the surgery of the ruptured male urethra it is accepted practice to divert the urine by suprapubic cystotomy (Herman, 1938; Badenoch, 1953; Poole-Wilson, 1956; Page, 1958)—and where possible to avoid the use of an indwelling catheter unless its splinting effect is indispensable, with the object of reducing subsequent stricture formation to a minimum. However, although there is agreement about suprapubic drainage, there are differences of opinion with regard to the harmful effect of the presence of a catheter. Trafford (1955) in a review of 32 cases of rupture of the posterior urethra states that "there is nothing to support previous theories that prolonged catheterization produces stricture" and is of the opinion that "it actually helps in its prevention".

As the anatomy and structure of the male and female urethra differ so widely, it may even be that the principles of treatment applicable to the male are inappropriate to the female, and drainage *via* an indwelling catheter in this case can at least be said to have so far been justified by the result, and to have the merit of simplicity.

Summary

A case of complete traumatic division of the female urethra is described.

The literature is briefly reviewed, and the management discussed.

Acknowledgment

My thanks are due to Mr. Anthony W. Purdie for permission to publish this case.

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IRREDUCIBLE PROLAPSE AND ITS TREATMENT

With a Report on Two Cases

BY

PREMA M. NAIDU, M.D., F.R.C.S.E., F.R.C.O.G.
Professor of Obstetrics and Gynaecology

AND

UMESH N. REDDY, M.D.
Gynaecological Registrar
Osmania Medical College, Hyderabad, A.P.

IN the city of Hyderabad, the incidence of genital prolapse, as met with at the gynaecological out-patient department of the Government Maternity Hospital, is between 7 and 8 per cent. The women here invariably carry on with their incapacities, whether they be vaginal bleeding or genital prolapse, for a long period before seeking relief. Hence cases of prolapse are seen not infrequently in an irreducible state associated with massive descent. In these cases none of the commonly accepted surgical procedures would be deemed suitable. The inverted vaginal walls are not only much hypertrophied and vastly increased in area but have harboured some of the abdominal contents over several years.

Colpectomy with vaginal hysterectomy as advocated by Phaneuf (1935, 1950), Williams (1950), Adams (1951), and as practised by Svesko (1958), was considered as a possible answer to some of the large and complicated cases of genital prolapse. With this in view, two such cases were investigated and treated. The two case reports and results are presented below.

Case 1 (12311), aet. 60 years, was admitted on 19th August, 1958 with the history of a mass protruding from the vagina for 10 years. She came in complaining of ulceration and bleeding which had been noted for a few days. She did not suffer from any disturbance of micturition or defaecation. The woman had had four normal live children born at term, at intervals of two years each. The last delivery took place 20 years ago. The menopause had commenced 12 years before. The patient was a public road sweeper requiring to work for hours on her feet. Examination of the mass (Fig. 1) revealed it to be a large genital prolapse, 20 cm. in length, 14 cm. antero-posteriorly and 15 cm. transversely. There was an ulceration about the middle on the right side covering an area of 7×8 cm. The mass consisted of a large cystocele and an enterocele with a number of loops of intestine that could be palpated in it, while its apex was formed by a small uterus. No reduction was possible. The cardiovascular system showed nothing abnormal. Her blood pressure was 140/100 mm. Hg, and the blood urea was 30 mg. per cent, while the red cell count and haemoglobin were satisfactory. A barium meal series showed the loops of small intestines (Fig. 2) lodged clearly in the prolapse. An intravenous pyelogram revealed dilated ureters which had been drawn down into the prolapse (Fig. 3). A sound showed the length of the uterus to be about 6 cm. The skin on the groins and thighs was sodden.

The patient went in and out of hospital for the treatment of the ulceration. But no suitable operative procedure could be decided upon to correct her prolapse till a year after her first admission.

FIG. 1

Picture showing a large irreducible genital prolapse.

FIG. 2

Barium meal film revealing loops of small intestines in the enterocele.

FIG. 3

Intravenous pyelogram showing dilated ureters drawn down into the prolapse.

FIG. 4

Picture taken 13 months after operation, showing appearance of perineum and shallow vagina.

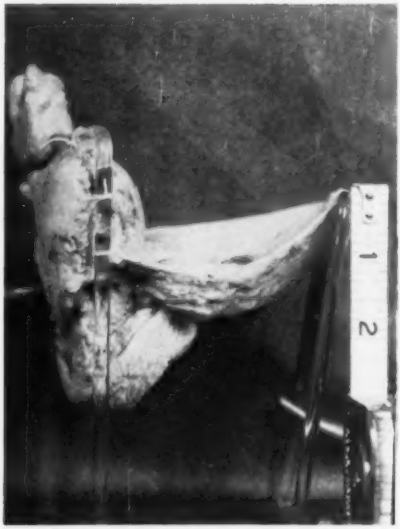

FIG. 5

Specimen of uterus and the hernial sac.

On 11th November, 1959, under spinal anaesthesia, colpectomy with vaginal hysterectomy was carried out. The special features noticed during the operation were the considerable bleeding met with during the stripping of the vaginal walls, and the ease with which the loops of small bowel could be returned into the abdomen. The uterus was small and when opened was found to contain two endometrial polypi. After the peritoneum was closed, the pedicles were brought together. Then the pubococcygeus muscles were apposed with interrupted 2/0 chromic catgut sutures.

On the 7th post-operative day, the Foley's catheter was removed and the patient was allowed to sit up. The perineum was slightly oedematous, but by the 10th day it appeared well healed and firm. There were no signs of pressure when she sat up. The patient was discharged two weeks later to return to her arduous work. The appearance of the shallow vagina and perineum thirteen months after operation is shown in Figure 4.

Case 2 (18458), aet. 55 years, was admitted on 15th December, 1958, with a complaint of a large mass projecting from the vagina for 10 years. She used to be able to replace it but it had become irreducible for about 4 years. She suffered from difficulty in micturition occasionally, and was relieved by pushing up the mass as far as she could. Her bowels were regular. She had menstruated regularly till her menopause 6 years ago. She had had 7 normal deliveries at term, at intervals of three years. Her last child was born 15 years ago.

The prolapse measured 18 cm. by 10 cm. The external os was like a small slit. The uterine canal measured 8 cm. There was complete eversion of the vaginal walls with a large cystocele and enterocele associated with general prolapse (Malpas, 1955). The barium meal revealed loops of small bowel in the mass in this case as well. The ureters were noted to be dilated in an intravenous pyelogram but they were not easily visualized in the prolapsed mass.

Since we were dealing with a large irreducible prolapse in a woman past the menopause, partial colpectomy with vaginal hysterectomy was carried out under spinal anaesthesia. Interesting features met with during this operation were the very moderate blood loss and the very large peritoneal sac (Fig. 5) that was easily excised. The pubo-coccygeous muscles were brought together satisfactorily. This patient was up on the 8th day. There was mild urinary infection during the post-operative period. The perineum on discharge on 18th day had healed soundly, the vagina was shallow and hardly 2 cm. deep.

Comments

It has already been stated that irreducible genital prolapse is not uncommonly seen here for which none of the standard surgical procedures are found to be suitable. These women are long past the child-bearing age and menopausal. The enterocele in the prolapse is unusually prominent and, due to the size and long duration, the vaginal walls tend to ulcerate. Perforation through the sac and intestinal obstruction have been reported by Daley and Callum (1946) and Thompson (1948). Even after a vaginal hysterectomy of the Mayo type, unless the resulting vaginal canal is deep, we can sometimes get rupture of the vault (Scott, 1955). Colpectomy results in complete closure of the hiatus urogenitalis by means of the pubococcygeous muscle and the pelvic floor support thus provided has proved to be very sound. It is believed with some evidence that even marital life is not impossible after colpectomy.

Despite the displacement and dilatation of the ureters noted in both the cases it is interesting to note the normal blood urea readings.

Conclusions and Summary

(1) We present two cases of massive irreducible genital prolapse treated by colpectomy combined with vaginal hysterectomy.

(2) Investigations showed that the ureters were displaced from the normal course and had undergone dilatation. The enterocele had several loops of bowel as revealed in the barium meal series.

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EARLY PRIMARY ABDOMINAL (POUCH OF DOUGLAS) PREGNANCY

With a Report of a Case

BY

L. IFFY, M.D., F.F.O.G.(Budapest), L.R.C.P.&S.(Edin.), L.R.F.P.S.

Locum Tenens Registrar, Obstetrics and Gynaecology

Kent and Canterbury Hospital, Canterbury

ALTHOUGH several hundreds of cases of abdominal pregnancy have been recorded in the medical literature, the number of those cases that fulfil Studdiford's (1942) requirements* accepted by Novak (1947) as criteria of "primary abdominal pregnancy", hardly reach a two-figure rate. The following report therefore, presenting the intact specimen of a very young product of conception recovered from the abdominal cavity, seems to be suitable for reporting.

CASE HISTORY

Mrs. D.M. (Reg. No. 4445/52), aged 28 years, British-born, was admitted as an emergency on 2nd November, 1959, at 6.20 a.m. She was complaining of severe abdominal pain which started at 2 p.m. the day before, immediately following a bowel-action which to her felt incomplete. The pain at first was localized to the suprapubic area, but later spread upwards and became more diffuse. From this time the micturition was painful and by 8 p.m. she could not pass water at all. She vomited three times after 10 p.m. At the time of her admission the pain was maximal and prevented her breathing deeply; she described it as "sharp" and "colicky". In respect of her general condition she only stated that she felt tired.

Past History. Apart from an appendicectomy about 12 years earlier she had enjoyed good health. Her periods were regular (5/28) and the births of her 3 children, the youngest of whom was 2-years old, were uneventful. Her last period started on the 3rd October and appeared normal in all respects. She noticed a "colicky pain in the womb" on about the 18th October which lasted for about 6 or 7 days, then disappeared. No vaginal bleeding or discharge had occurred since her last menses.

The patient looked ill and anaemic. The tongue was clean and moist. The temperature was 98·6°. There was tenderness all over the abdomen and generalized guarding was detected. There were no localizing signs. Bowel sounds were infrequent and normal. Rectal examination revealed a soft, boggy feeling in the pouch of Douglas with tenderness of the pelvic organs. The heart was normal by auscultation and by percussion. The blood pressure was 120/75, the pulse 96/minute, regular. The urine was clear. The haemoglobin was 70 per cent (10·4 g./100 ml.). Blood group O Rh positive.

Gynaecological examination. The external genitalia and vagina were normal. The cervix was healthy and of normal colour. On bimanual examination the pouch of Douglas was bulging, exquisitely tender and so were the anterior and lateral fornices and the whole lower abdomen. An ill-defined, small tumour could be felt in the middle of the pouch of Douglas, but the uterus could not be separately defined due to generalized guarding. Percussion of the abdomen did not reveal free fluid in the cavity. The patient was restless and unco-operative.

8.30 a.m. Blood pressure: 110/70 mm. Hg. Pulse rate: 100/minute. Regular, but of small volume.

9 a.m. Gynaecological examination under

* Studdiford's criteria: (1) the tubes and ovaries must be intact, (2) there must be no evidence of utero-peritoneal fistula, (3) the pregnancy must be young and related to the peritoneal surface only.

pentothal $-N_2O$, $-O_2$ anaesthesia. The small, anteflexed and anteverted uterus was clearly defined. An indeterminate tumour was felt in the pouch of Douglas but both adnexa appeared clear.

Puncture of the pouch of Douglas revealed fresh blood containing a few small clots in the abdominal cavity.

Operation. Together with simultaneous blood transfusion the abdomen was opened by a low, median incision. About 900 ml. of fresh blood was found in the abdominal cavity, but surprisingly both Fallopian tubes appeared intact, perfectly healthy and mobile, the uterus was of normal size, healthy, anteflexed and anteverted, the ovaries were of normal appearance. After careful removal of clots from the pouch of Douglas a small, bleeding tumour could be seen, which was attached to the peritoneum, but could easily be wiped off its base, leaving behind a raw, bleeding surface of about 2–3 cm. in diameter; it was situated on the surface of the rectum and partly on the neighbouring peritoneum of the pouch of Douglas. The bleeding stopped after this area had been closed with a transverse suture-line of No. 00 catgut. A cyst of Morgagni was removed from the back of the left broad ligament and the abdomen was closed in layers.

Following the operation a further two pints of blood were given. The patient had a temperature of 102·2 a few hours later. The temperature gradually fell to 100·0 by 48 hours after the operation and to a normal level by the 5th day. The Hb. was 80 per cent on the 5th and 85 per cent on the 7th day. All clips were removed on the 5th and sutures on the 7th day and the patient was discharged home on the 16th post-operative day after an uneventful recovery.

Pathological report. "Received (1) a small, round, thin-walled simple cyst of broad ligament measuring 1·8 cm. in main diameter; (2) an ectopic pregnancy with complete sac and embryo measuring approximately 1·2 cm. in length, aged approximately 4–5 weeks."

Re-examination of patient on the 31st December, 1959. Cervix, fornix and both adnexa appeared normal. The uterus was of normal size and mobile. The patient had no complaint since leaving the hospital.

Discussion

The above-described case shows striking similarity to that of Martini (1957), who, in his case report, presented a detailed description of the site of implantation, which was the peritoneum of the pouch of Douglas and the surface of the rectum. This abdominal pregnancy produced a serious internal bleeding only 3 days after the patient's first missed period. Taking into account Myles' (1954) and Nicolson's (1947) remarkably similar cases where the pregnancy ended 7 and 10 days after the missed period and also the fact that such early termination is extremely rare among abdominal ectopic pregnancies it seems justifiable to conclude that primary pouch of Douglas pregnancies are likely to cause early disaster in the abdomen. The topographical conditions offer a good explanation for this phenomenon; when one part of the products of conception is anchored to the peritoneum of the immobile pouch of Douglas, while the other end is pulled and stretched by its attachment to the mobile and motile rectum. The above history of bowel action closely followed by the onset of abdominal pains seems to furnish strong evidence in favour of this explanation.

The question, whether those abdominal pregnancies considered as "primary" by Studdiford, Novak and many others really result from primary abdominal implantations is still open to discussion. Nicolson drew attention to the fact, that his patient had severe abdominal pain two weeks before her missed period and suggested that this pain might have been due to a tubal abortion followed by secondary implantation of the embryo on the peritoneal surface. He considered therefore his case as one of secondary origin, although it was a primary one in Studdiford's terms. Here the patient gave exactly the same history and this fact strengthens his explanation in respect of the pathological mechanism of the peritoneal implantation.

Those abdominal pregnancies where the product of conception gradually protrudes through the abdominal opening of the Fallopian tube and where the placenta gets attached to the peritoneum form the clearly defined group of "secondary abdominal pregnancy". The

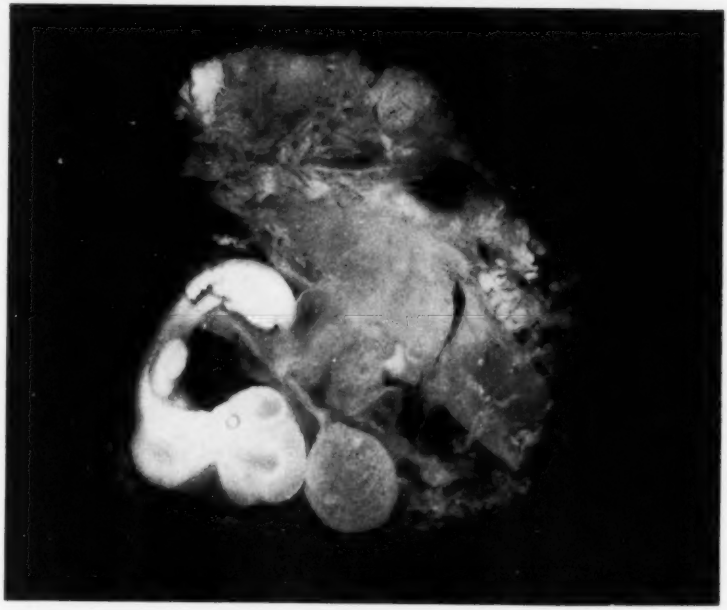

FIG. 1

Specimen of an early primary abdominal pregnancy. Estimated age of the embryo: approximately 4 weeks. ×3.

few scattered examples of "true" primary abdominal pregnancies, however, so far have failed to produce sufficient evidence about their origin.

Acknowledgments

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MULTIPLE RETROPERITONEAL SMOOTH MUSCLE TUMOURS

A Report of Two Cases Treated by X-rays

BY

D. H. BLAKEY, M.B., M.R.C.O.G.
Lecturer in Obstetrics and Gynaecology
University of Sheffield

THE border-line between benign and malignant neoplasms is sometimes poorly defined, whether judged by histological appearance or clinical behaviour. It is a feature of tumours of smooth muscle origin that the diagnosis of malignancy is notoriously difficult (Steiner, 1939; Cowdell, 1950; Willis, 1953; Novak, 1958). Though the myoma is one of the most common of all human tumours, it is much less frequent outside the uterus. The retroperitoneal site is the least common but the most unfavourable because diagnosis is difficult and treatment unsatisfactory. They are usually single growths, often attaining a large size, and producing symptoms only from direct pressure on neighbouring structures. Their situation often makes surgical removal hazardous or even impossible, and unfortunately X-rays are said to have no appreciable effect upon them (Golden and Stout, 1941; Cowdell, 1950). If untreated they continue to grow and eventually terminate fatally, though their degree of malignancy is generally lower than that of most sarcomata. The following two cases are reported because of their unusual clinical features, the illustration they present of the borderline between malignancy and benign behaviour, and for the thoughts provoked by one of them about the origin of uterine fibroids.

Case 1

Mrs. P.S., a para-1, aged 37, was seen in July, 1952, complaining of pain in the left side for two years, increasingly heavy menstrual periods since their onset at the age of 16, and swelling of the abdomen. She gave a history of one normal birth 12 years before, followed 3 years later by the removal of a fibroid by myomectomy at the age of 28. Her symptoms at that time were very similar to those now presenting. On examination an irregular, firm swelling could be felt rising from the pelvis reaching to the umbilicus. Bimanual palpation confirmed gross uterine enlargement, and a diagnosis of multiple uterine fibroids was made. Admission for hysterectomy was advised.

When the abdomen was opened on 26th July, 1952, an inoperable growth of remarkable characters was found. The uterus was distorted by a large irregular mass which filled the pelvis and extended to the lateral pelvic walls. There were dense adhesions between the mass and bowel and peritoneum so that the pelvic cavity was completely obliterated and the ovaries could not be seen. In addition there were a great many growths scattered about the rest of the abdomen, arising largely from the parietal peritoneum. They were firm, globular swellings, reddish-brown in colour, often pedunculated, with a leash of alarmingly large vessels running over the surface of each of them. They resembled uterine fibroids but were as soft as a pregnant uterus. In size they varied between 2 cm. and 10 cm. in diameter. No visceral masses were seen; in particular the liver, stomach and aortic glands were normal. The condition was thought to be malignant—probably a sarcomatous change in uterine fibroids—and was certainly inoperable. The largest mass within convenient reach, from the parietal peritoneum above the upper end of the paramedian incision, was excised for histological study, and the abdomen

was closed. Recovery from operation was uneventful, and she returned home on the 12th day.

The pathologist reported that the tumour appeared to be a leiomyoma which had undergone gross myxomatous degeneration and cystic change. No evidence of malignancy could be found in the sections examined (Fig. 1).

Sections of the original fibroid removed in another hospital in 1944 have recently been traced, and the diagnosis of a simple uterine fibromyoma confirmed. There were no unusual features.

When seen 2 months after operation the patient was well, but still complained of dragging abdominal pain. The mass in the lower abdomen was unchanged. After prolonged review of the problem, during which consideration was given to re-operation, but rejected, it was decided to try the effect of deep X-ray therapy to suppress ovarian function. In December, 1952, 5 months after operation, super-voltage X-rays were given on three successive days to a total depth dose to the pelvis of 700 r. (this is rather higher than the usual "sterilizing dose" of 400 r.). The patient was observed closely as an out-patient, and 6 weeks later the mass was found to be smaller. Its size was reduced steadily at each examination, until by December, 1953, one year after treatment, it had disappeared altogether. Apart from minor oestrogen withdrawal symptoms, easily controlled, she remained well, and subsequent annual examination has failed to reveal any recurrence. She was last seen on 7th April, 1960, 7½ years after operation. She looked and felt extremely well; her weight was 142 pounds (64·5 kg.), and on pelvic examination a normal, mobile, anteverted uterus could be felt, without any evidence of abnormal masses elsewhere. There had been no bleeding since a few months after the X-ray menopause.

Case 2

Mrs. M.C., a para-3, aged 65, was referred to the University Department of Medicine with a variety of complaints including malaise for several years, pain in the lower abdomen, breathlessness, and, for the previous 12 months, discomfort "down below" on sitting down. Vaginal and rectal examination revealed a large smooth, hard lump filling the Pouch of Douglas, and a smaller, separate mass the size of a small orange reaching down to 1 inch (2·5 cm.) above the introitus. She gave a history of "removal of a lump between the bladder and rectum" 7 years earlier, but it has not been possible to trace further details. She was an introspective, anxious type of woman, who had previously spent some time on the medical wards with a diagnosis of "cardiac neurosis". She was admitted for laparotomy on 1st October, 1957.

The pelvic cavity was found to be obliterated by dense adhesions of large gut to a mass about the size of a foetal head arising from the pelvic floor. During dissection to expose the tumour more fully, an abscess cavity was opened and further exploration was therefore abandoned in that area. A segment of the exposed surface of the tumour was removed for biopsy. Three fusiform masses were palpated in the upper abdomen. They were of firm consistency and about the size of hen's eggs, situated in relation to the transverse colon and stomach. The condition was diagnosed provisionally as malignant and inoperable, and the abdomen was closed. The tumour in the recto-vaginal septum was removed entire for more detailed study as it was the most easily accessible of the various tumours found. It was excised by the vaginal route; it was encapsulated in close proximity to the rectal wall.

Preliminary microscopic examination suggested that it might be a neurofibroma, and the patient was re-examined for evidence of von Recklinghausen's disease. A pigmented "mole" was excised from her back under local anaesthesia, but on section proved to be a simple inclusion dermoid. On more careful study of the original sections, the diagnosis was revised to leiomyosarcoma. The pathologist reported a pleomorphic tumour. The nuclei were for the most part spindle-shaped but there was considerable variety in size and staining properties. A few giant cells were present and mitoses were frequent. The nuclei tended to arrange themselves in palisades with an intervening cytoplasm in which faint fibrillae could be demonstrated. Although there was a superficial resemblance to a neurofibroma, the nuclear irregularity and fibrillary nature of the cytoplasm and the absence of collagen indicated that this was a leiomyosarcoma (Fig. 2).

The patient made a normal recovery from operation, and, in view of the revised diagnosis, a course of supervoltage X-ray therapy was

given. A total depth dose to the pelvis of 3,110 rads was given in 18 doses over a period of 37 days during November and December, 1957. A barium meal showed no fault in the stomach or transverse colon at that time, and no opacities were seen on X-ray of the chest. She has remained reasonably well since, though she was admitted to the medical wards in September, 1959 with a haematemesis. A barium meal then showed a filling defect in the pyloric antrum consistent with a gastric neoplasm. No change could be detected in the pelvic findings since operation 2 years earlier. The recto-vaginal tumour had not recurred. Palliative management was advised in view of the malignant features of the original tumour, and she has since maintained quite reasonable health. In fact her general condition remains remarkably good. There has been no loss of weight and no metastases could be seen on a recent chest X-ray. She was last seen in March, 1960.

Discussion

Incidence

The gastro-intestinal tract is the commonest site for smooth muscle tumours outside the uterus. Golden and Stout, in their classic review published in 1941, suggest that this cause should be suspected in all cases of gastro-intestinal haemorrhage of uncertain origin. They found that retroperitoneal growths had been reported only 43 times out of a total of 1,018 cases (4·5 per cent) described in 400 publications reviewed by them. They stress the high proportion of malignancy of myomas in this situation and the almost inevitable fatal outcome in the untreated case. In fact they describe a case of spontaneous regression in an inoperable retroperitoneal smooth muscle tumour in a woman of 44 who refused X-ray therapy, and who was symptom free 7½ years after laparotomy, and claim that it is the only one of its kind on record.

It is evident therefore that the 2 cases presented have a number of unusual features: the first had metastases without clinical or histological evidence of malignancy, and regressed dramatically after a "sterilizing dose" of X-rays, whereas the second, though histologically malignant, seems to be running a fairly benign course 2½ years after X-ray therapy—though this is consistent with the low grade malignancy previously reported in this type of tumour.

A search of the literature has revealed a report of a single case of multiple retroperitoneal tumours very similar to the first one described in this paper (Willson and Peale, 1952). It is a remarkable coincidence that it was published in July, 1952, the very month in which the present case was operated upon. As far as can be ascertained these are the only two such cases ever recorded in the English language.

Malignancy

The most convincing clinical evidence of malignancy is the presence of metastases, and in the case of smooth muscle tumours these are usually found in the lungs and liver (Steiner, 1939; Novak, 1958). Uncertainty about the histological diagnosis of malignancy is notorious, but most authors agree that the frequency of mitoses is the most reliable index (Golden and Stout, 1941; Novak, 1958). It is the occurrence of cases of smooth muscle tumours on the borderline of malignancy, where disparity exists between clinical and histological features, that has led to a confused nomenclature using such terms as "recurrent fibroids", "malignant myomata", "metastasizing leiomyomata", etc. Willis (1953) makes the comment, ". . . but a tumour which invades or metastasizes is a sarcoma however well differentiated is its structure". When dealing with borderline cases generalizations are liable to be misleading; this is illustrated by the first of these cases in whom such apparently obvious metastases were related to a completely benign structure, and whose subsequent behaviour fully supports the fundamentally benign nature of the lesion. It seems that this was a hormonally dependent tumour which regressed when ovarian activity was suppressed with a relatively small dose of supervoltage X-rays.

Aetiology

There has been much speculation on the significance of hormonal influences on ordinary uterine fibroids, but no simple relationship seems to explain the observed facts (Witherspoon, 1933, 1935; Goodman, 1946; Burrows, 1949). It is likely that the tendency to develop fibroids

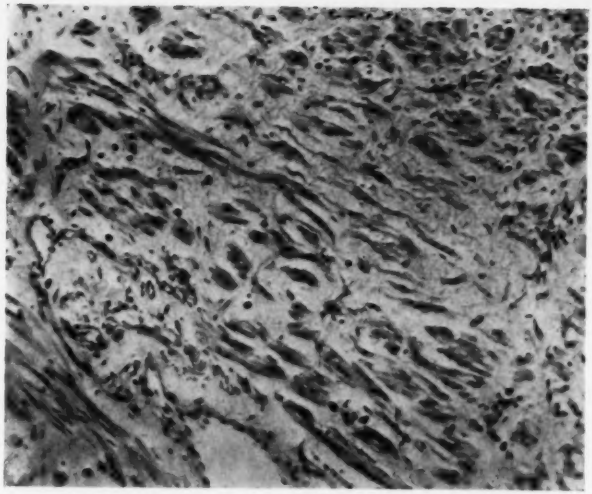

FIG. 1

Low power view of section from the fibroid mass removed from Case 1. Leiomyoma showing myxomatous change.

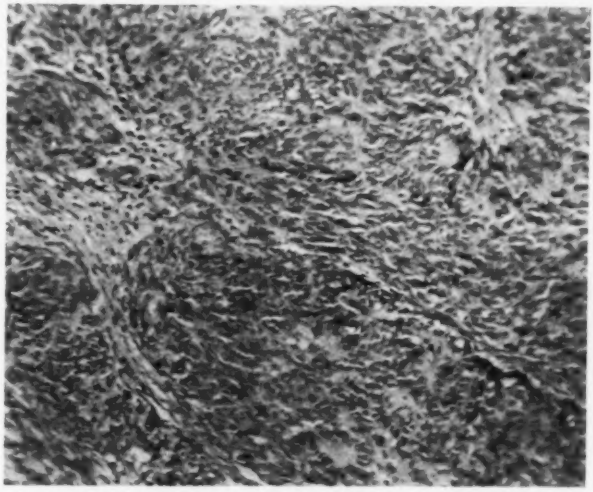

FIG. 2

Low power view of section of tumour removed from recto-vaginal septum in Case 2. Considerable variety in size and staining properties of nuclei, with a few giant cells and frequent mitoses, together with fibrillary nature of cytoplasm and absence of collagen, indicate that this is a leiomyosarcoma.

differs widely from one person to the next, and the patient here described may represent an extreme of biological variation in which the host was unusually susceptible to ovarian hormones.

There is a striking similarity between this case and the experimental tumours produced in castrated female guinea-pigs by the injection or implantation of large doses of oestrogens, 100–150 times greater than physiological amounts, so extensively investigated by Lipschütz and Vargas (1939, 1941). Though these experimental tumours differed histologically from naturally-occurring uterine fibroids and were scattered throughout the abdominal cavity, they resembled the present case in their benign cellular structure, and their spontaneous regression after removal of the stimulating hormone. These observations lend support to hypotheses about hormone imbalance, especially excess oestrogen production unrestrained by normal progesterone output (Burrows, 1949).

It is of great interest that oestrogen excess was demonstrated in Willson and Peale's case (1952) by the presence in one ovary of a small granulosa cell tumour. Their patient was a woman of 38, who had been treated by subtotal hysterectomy for fibroids at the early age of 27. The cervical stump, both appendages and all accessible myomatous masses, 36 of which formed a cluster arising from a localized portion of the omentum, were removed. The granulosa cell tumour was discovered on histological examination, the ovary containing it being enlarged to only 1½ times its normal size. A corpus luteum was seen in one ovary, but no progestational change was found in some remaining endometrium, and they suggest that the oestrogen level may have been so high that the corpus luteum effect was not demonstrable. The sections of the fibroid masses showed identical features to those described in the Sheffield case, including myxomatous degeneration. The representative sections are astonishingly similar.

The distribution of the growths does not suggest direct spread from the parent tumour in the pelvis, though occasional case reports indicate that unexpected routes are possible. For example, Marshall and Morris (1959) describe a case of direct intravenous extension of soft myomatous tumours on a massive scale along the course of grossly dilated ovarian veins. Their patient remained well and symptomless 16 months after simple hysterectomy, though substantial masses were left *in situ* above the level of the pelvic brim.

The most likely explanation would seem to be a multifocal origin, as in Lipschütz's experimental animals, from mesenchymal tissue. Presumably smooth muscle elements are capable of growth wherever they are situated provided they are sensitive and suitably stimulated. It is apparent that both the women who developed such large numbers of retroperitoneal "metastases" were highly "fibroid-prone", as they had both undergone previous conservative operations for fibroids in their late 20s, several years before developing multiple retroperitoneal growths.

Treatment

The effects of simple "sterilizing dose" of X-rays was dramatic in the first case, exceeding all reasonable expectation, and was clearly much to be preferred to a hazardous operation, even had this been judged possible. To what extent the lack of clinical deterioration in the second case can be attributed to X-ray therapy is more difficult to say. Leiomyosarcomata are often of low malignancy and the patient's present condition is not inconsistent with a natural course of the lesion, though more rapid recurrence of the local tumour in the recto-vaginal septum was anticipated. X-ray therapy has been stated to have no appreciable effect upon these tumours, and surgery is the only possible line of treatment (Golden and Stout, 1941; Cowdell, 1950), but where operation is deemed unsafe, it would seem to be well worthy of trial. Nothing has been lost by its use in the two cases described, and in one a great deal has been gained.

Summary

Two inoperable cases of multiple retroperitoneal smooth muscle tumours are described. One consisted in widespread pedunculated tumours from the parietal peritoneum remote

from the uterus which was distorted by similar growths. The tumour in the latter case was histologically benign, and regressed completely following a sterilizing dose of X-rays. Only one other similar case has been traced in the literature.

The difficulties of diagnosis and prognosis are briefly discussed.

X-ray therapy, though usually condemned as valueless, appears to have been of considerable help in at least one of the cases.

I wish to thank Mr. L. B. Patrick, F.R.C.S., F.R.C.O.G., for permission to describe the first case, who was admitted under his care, and Dr. C. G. Paine, M.D., for the histological reports and photomicrographs.

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FIG. 1

TORSION OF FALLOPIAN TUBE

Report of a Case

BY

C. S. LYGONIS, M.D.

St. Giles' Hospital, London

BECAUSE of the rarity of the condition a case of torsion of Fallopian tube is presented.

CASE REPORT

A married woman, 42 years of age, was admitted to St. Giles' Hospital on the 12th February, 1960, complaining of severe intermittent colicky abdominal pain, radiating down to the right thigh, which started suddenly about 18–20 hours earlier. She had vomited six or seven times since the attack of pain.

On examination she was pale, temperature 97°, pulse rate 90, blood pressure 140/95.

Chest and cardiovascular system—no abnormality detected.

Abdomen—no distension, slight guarding on the right iliac fossa and very tender.

Per rectum—no abnormality detected.

Micturition—normal.

She stated that the monthly period had been always regular; last period was 10 days before.

A diagnosis of renal colic was made, but straight X-ray of the abdomen showed no calculus.

A few hours later the pain became worse, the pulse rate increased to 120, the lower abdomen appeared rigid. A provisional diagnosis of torsion of small ovarian cyst or ectopic gestation was made and laparotomy under general anaesthetic proceeded with.

There was free blood in the peritoneal cavity, the right Fallopian tube was found to be twisted anti-clockwise and was distended with blood. Right salpingo-oöphorectomy was performed.

Post-operative recovery was uneventful. There was vaginal blood loss for the first 5 or 6 post-operative days.

The specimen (Fig. 1), consisted of the Fallopian tube, which was about 8 cm. long and engorged with blood. The ovary was also congested. Section showed the whole of the Fallopian tube to be intensely congested. There was no evidence of retained products of conception. The appearance was of torsion of the Fallopian tube.

DISCUSSION

Torsion of the Fallopian tube is a rare condition and is very difficult to diagnose pre-operatively because there are no characteristic clinical symptoms, especially when the tube is known to be healthy.

The first case was reported by Bland-Sutton (1890). Since then over 200 cases have been reported in the world's literature.

Many theories exist about the mechanism and aetiology of torsion of the tube, but none is very convincing. Blum and Sayer (1937) have fully discussed the subject. The symptoms may resemble torsion of ovarian cyst, salpingitis, ectopic gestation, appendicitis or ureteric calculi, making the diagnosis almost impossible pre-operatively.

The usual symptoms are sudden severe pain in an iliac fossa with tenderness locally, nausea and vomiting. The temperature is usually normal.

SUMMARY

A case of torsion of the Fallopian tube is presented, in which torsion occurred in a previously healthy tube.

My thanks are due to Mr. Iain Matheson for his help with the script and to Dr. E. M. Bailey for his help with the photograph.

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ANTENATAL DIAGNOSIS OF CONGENITAL HEART BLOCK

BY

H. P. DUNN, F.R.C.S., M.R.C.O.G., F.R.A.C.S.

Assistant Obstetrician and Gynaecologist

National Women's Hospital, Auckland, New Zealand

IT is distinctly unusual to diagnose twins at 30-weeks maturity and to know that one of them will have congenital heart disease. According to Redman (1958) only 13 cases of congenital heart block had been diagnosed before delivery and later confirmed by electrocardiography. McNie and Johnstone (1959) also found 13 cases in the literature and added one of their own, diagnosed at 39 weeks. After eliminating the cases common to both articles there appear to have been at that time a total of 23 reported cases. Connor *et al.* (1959) described a further one diagnosed at 39 weeks, and the present case makes the 25th. It is the earliest diagnosis of the condition yet recorded, and the only one involving twins.

CASE REPORT

Mrs. T.A.H., a 24-year-old primigravida, was first seen on 29th September, 1958, at 22-weeks maturity. She had had her last menstrual period on 28th April, 1958, and had felt quickening on 29th August, at 17 weeks. On 24th November, at 30 weeks, two distinct foetal hearts were heard, one whose rate was 52 being located in the right upper quadrant of the uterus, while the other was found in the left lower quadrant at the rate of 150; the maternal pulse rate was 78. At the next antenatal visit on 8th December the slow heart could not be heard clearly and the diagnosis was held in doubt, but on 22nd December, at 34 weeks, the slow heart was again heard with ease. On the next day a foetal electrocardiograph (Figs. 1 and 2) was made and the diagnosis of twins, one with heart block, was confirmed.

There had been no infectious disease or other abnormality in early pregnancy, and no X-rays had been taken. In the week before delivery a systolic murmur could be heard in the slow heart. The mother's blood pressure range was between 110/60 and 120/80, and there was no albuminuria or oedema. From the 22nd to the 40th weeks the total weight gain was only 4 pounds (1·8 kg.). Her weight fell from 9 stones 9 pounds (61·4 kg.) at the 32nd week to 9 stones 4 pounds (59·1 kg.) at term. As she was in some distress, with difficulty in moving about, and, as her general condition was deteriorating, labour was induced at term in Wakefield Private Hospital by low rupture of the membranes, on 3rd February, 1959.

On 4th February, after some 12 hours of labour, she had a spontaneous delivery of the first (normal) baby by the vertex, and 20 minutes later there was an assisted breech delivery of the second. The first infant was a boy weighing 5 pounds 15 ounces (2,730 g.) and his respirations were established immediately. He made normal progress thereafter. The second was also a boy, weighing 4 pounds 12 ounces (2,250 g.). He showed asphyxia livida with gasping respirations for about 10 minutes, but his colour gradually improved and cyanosis did not recur after the first 12 hours. His heart rate varied from 50 to 54, and the rhythm was regular. A prolonged systolic murmur of moderate intensity was present at all areas, and this was taken to indicate a patent interventricular septum. An electrocardiogram showed that the heart block was complete (Fig. 3). The placentae were separate, and both appeared normal.

At 12 weeks the first twin was thriving and weighed 12 pounds (5·5 kg.). The affected child was 8 pounds (3·6 kg.) and although there was no cyanosis the breathing was laboured during feeding. At 11 months the first weighed 22 pounds (10 kg.) and was crawling, while the second was 15 pounds (3·2 kg.). He was sitting up but not moving about. There were no cyanotic attacks but he had pallid episodes and was very lethargic.

At 13 months the affected twin weighs 17 pounds (7·7 kg.), is a slow feeder, does not crawl, and is generally lethargic. He has episodes of pallor but no cyanosis. The heart rate is 52, and the murmur is unchanged. The normal twin is 23 pounds (10·4 kg.).

DISCUSSION

While the diagnosis is by no means difficult, especially if antenatal foetal electrocardiography is available, recognition of the condition before labour is important in that it would deter one from adopting heroic measures in the manage-

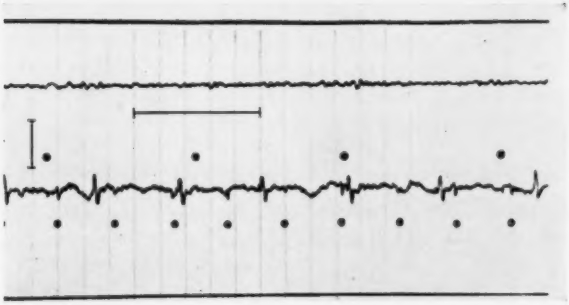

FIG. 1

Antenatal foetal electrocardiogram at 34-weeks maturity. The vertical scale indicator represents 50 microvolts, and the horizontal scale 1 second. The mother's QRS complexes are easily seen, the rate being 84. The black dots above the tracing point out QRS complexes of the twin with heart block, regularly recurring at a rate of 50. The lower line of circled dots indicates the QRS complexes of the normal twin, whose heart rate is 144.

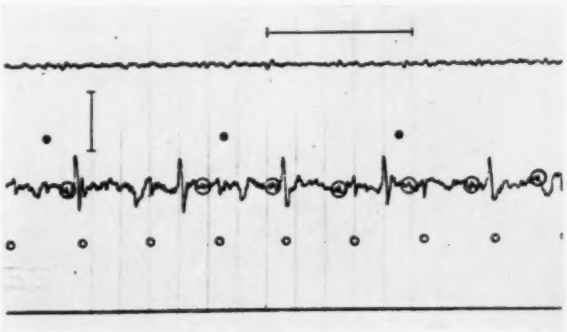

FIG. 2

This is a different part of the same electrocardiogram as in Figure 1 with the P waves of the affected twin encircled on the tracing. Dr. Liley was able to find them appearing regularly at a rate of 120.

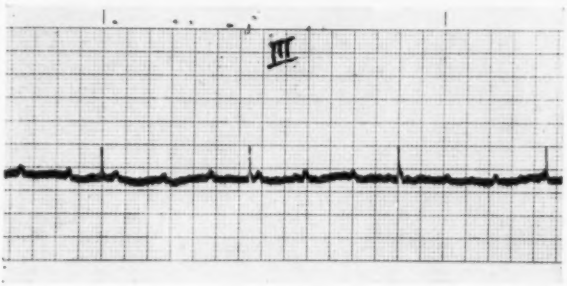

FIG. 3

Electrocardiogram of the affected twin, taken an hour after delivery, showing complete heart block.

ment of supposed foetal distress, and moreover the father can be warned in advance that some abnormality in the child could be expected. The prognosis is not always gloomy as some children with this condition grow to maturity with little or no limitation of exercise tolerance, but these are the exceptions. In most cases the heart block is due to an interventricular septal defect which interrupts the bundle of His, and this is not amenable to surgical correction. In other cases there may be Fallot's tetralogy, cor triloculare, transposition of the aorta, various other developmental anomalies, or there may be no anatomical lesion.

The cardiogram was taken with a Grass model electroencephalograph machine with frequency response modified so that only the higher frequency components of the electrocardiographic wave were recorded. The room was electrically screened to reduce interference. The electrodes were standard suction types, both applied to the mother's abdomen in the midline.

Acknowledgments

Thanks are due to Dr. A. W. Liley, of the National Women's Hospital, for recording and interpreting the electrocardiographs, and to Mr. J. Sloan for the photography.

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POST-MENOPAUSAL ENDOMETRIAL TUBERCULOSIS

BY

E. M. BARBOUR, M.D., M.R.C.O.G.

Assistant Gynaecologist

The Royal Samaritan Hospital for Women, Glasgow

POST-MENOPAUSAL endometrial tuberculosis is a relatively uncommon condition (Jameson, 1935; Towers, 1954; Sutherland, 1956). It appears to occur in that group referred to as unsuspected tuberculosis of the endometrium and, indeed, it was the microscopic appearance of a recent histological section at this hospital, which prompted the present study. The more frequent use of curettage as a diagnostic procedure accounts for the detection of the condition and it may be of interest to recount the findings in a series of 9 cases discovered in the last 30 years at the Royal Samaritan Hospital, Glasgow. Four were discovered in the years 1950–59 and, in the course of Sutherland and Garrey's (1951) general survey, a number of cases of pelvic tuberculosis in older women were found in the years 1930–49. From these, a further 5 cases of this particular condition were taken and I am grateful to Sutherland and to Garrey for permission to include them in this series.

The clinical details of the 9 cases are given in Table I.

PREVIOUS REPORTS

Towers (1954) quotes earlier reports on this subject listing some 24 cases in the world literature in the preceding 70 years. He also gives 8 reports in which 7 occurred in conjunction with carcinoma of the corpus and 1 associated with adenomyosis. Sutherland and Garrey (1951) found 7 cases in 65,943 admissions to the Royal Samaritan Hospital during the years 1930–49 (of which 5 were true post-menopausal endometrial tuberculosis and described herein). Sutherland and McBride (1954) found 1 tuberculous endometritis in 1,000 cases of post-menopausal bleeding; the histological specimen consisted of tuberculous granulation tissue. The patient was aged 46 and had had a natural menopause 19 years previously. Towers (1954) describes a case of tuberculous pyometra occurring in a woman of 73. Stallworthy (1952) encountered 1 case presenting as post-menopausal bleeding from a proliferative endometrium. Russell *et al.* (1951) found endometrial involvement in a woman of 60 complaining of post-menopausal bleeding; a tubo-ovarian mass was also present. McIntosh and Richmond (1959) reported 1, possibly 2, cases occurring in association with adenomyosis.

CLINICAL

Towers (1954) points out that the age distribution ranges from 46 to 90, almost half being between 47 and 55. In this respect, the present series is typical. Whether the post-menopausal cases represent a continuation of a disease process present in earlier life or whether the condition has arisen only in later life can only be assumed from the evidence of the fertility of the patients, the presence or absence of menstrual disorders in earlier life and whether tuberculosis has been found elsewhere in the body, either active or healed.

During the reproductive years, it seems generally agreed that endometrial tuberculosis is secondary to tubal disease carried by a haematogenous spread from a focus in the lungs or abdomen or, less frequently, bone, joints or

TABLE I

	Age	Puberty	Cycle	Menopause	Married	Children	Age of Last Child	Present Complaint	Other Evidence of Tubercle
1.	53	16	3/28	41	28	4	24	Prolapse; cystocele	20 years ago—ascites, X-ray chest—healed focus.
2.	47	14	4–5/28	46	20	0	—	Hypothyroidism	X-ray chest—a few calcified foci.
3.	51	16	4/28	50	22	2	18	Post-menopausal bleeding	Thickened right adnexa.
4.	63	14	2–3/28	53	—	—	—	Urethral caruncle	X-ray chest—healed minimal tuberculosis. Abdominal — scattered calcified glands.
5.	49	15	6/28	47	28	1	24	Leucorrhoea	Pleurisy 3 years ago.
6.	66	12	4/28	50	47	10	29	Post-menopausal bleeding	Appendicectomy 26 years ago; adhesions 12 years ago.
7.	62	15	7/28	49	30	4	23	Cervical erosion. Urethral caruncle. Deficient perineum	Losing weight, night sweats, cough.
8.	54	14	4/28	46	34	4	23	Pyometra. Epithelioma vaginae	Appendicectomy 17 years ago.
9.	62	—	—	45	38	7	23	Post-menopausal bleeding	Nil.

Incidence: 9 cases in 106,192 admissions in 30 years

peripheral glands. In the post-menopausal case, however, as Towers points out, there are two modifying factors: (1) the greatly diminished blood supply to the atrophying genital organs and (2) the absence of periodic shedding of the endometrium in menstruation. The first, he says, is partly responsible for the rarity of the condition in older women and the second, for the fibroid caseous tuberculosis seen in this age group.

Different factors have been mentioned as possibly favouring the development of genital tuberculosis—gonorrhoeal and puerperal infections, tumours and uterine hypoplasia. It is difficult to prove that former gonococcal or puerperal infection or tumours make the soil more inviting for the *Mycobacterium tuberculosis*. Some writers believe that uterine hypoplasia predisposes to the development of genital tuberculosis. Jameson (1935) reported that uterine hypoplasia was commonly found in genital tuberculosis basing his opinion on actual measurements of the uterine body. It cannot be stated, however, which comes first, the tuberculosis or the genital hypoplasia. The majority of women with pelvic tuberculosis have never conceived. Under these circumstances, the uterus would naturally be smaller than if it had functioned normally and borne children.

A study of the present series seems to indicate that the condition has arisen in later life. Seven of the 9 were parous, the endometrial involvement being detected between 18 and 29 years after the last pregnancy. There was no record that the puerperia were abnormal in any instance. With regard to uterine hypoplasia, only Case 7 had a uterine cavity described as "very small". The others had normal lengths with the exception of Case 9 in which the cavity was stated to be 1½ inches above normal. While searching for other evidence of tubercle, it is remarkable that we should find that most of the incidents in the present series appear to have succeeded the child-bearing interval although, of

course, the radiological signs of healed chest and abdominal foci give no indication of the duration of involvement of these two systems.

During the reproductive years, any menstrual disturbance appears to be in the direction of menorrhagia although the number is not significant (Russell *et al.*, 1951) and the impression is that there is no characteristic menstrual picture. Departures from the normal are probably not significantly greater than in the population of the same age group as a whole. This is explicable if it be remembered that the lesions are minute and found in any layer of the endometrium and at any phase of the cycle. It is only when the endometrium is largely replaced by tuberculous granulation tissue that gross departures from the normal menstruation may occur.

Stallworthy (1952) expressed the opinion that many patients with tuberculosis of the endometrium will heal naturally. While this may be so, Russell *et al.* (1951) pointed out that where the lesions are more superficially situated, they are more easily exfoliated during menstruation which is usually normal in such cases. This may account for some of the apparent "cures" in some cases whether treated or not. The fact that tuberculous lesions are infrequently encountered at the age when curettage is most often performed, namely, the menopause, is significant and may support the theory that spontaneous healing can occur.

The Table shows that the menstrual cycles of the present series had been normal. The events shown as "other evidence of tubercle" suggest that the endometrial involvement must have taken place, so far as the parous patients were concerned, some years after the last confinement but before the menopause and have persisted since. Had the infection occurred post partum, there would have been either an acute febrile illness or, at least, a persistent symptom—bleeding or abdominal pain—as has been described by Sutherland (1952) and Morrison and Ealand (1954). Both the age of these patients and the radiological evidence of healed foci suggest either a high degree of host resistance or a low virulence of the infecting organisms. Barns (1955) has estimated, in younger age groups, that endometrial involvement probably took place from months to 3 years after the primary infection elsewhere. Whether this is true also of the menopausal woman is impossible to tell. If, therefore, the patients became debilitated in any way towards the end of the reproductive years, the infection would eventually reach the endometrium by the haematogenous route. The co-incidence of diminished blood supply and cessation of "self-cleansing" menstruation following the menopause is a possible explanation for the persistence of endometrial involvement in the present series.

Clinical Pathology

According to Towers (1954), the actual lesion may take one of three forms. First, it may be part of a widespread tuberculosis involving the female genital organs and other structures in the pelvis. Secondly, it may occur as a gross infection involving the wall of the uterus but apparently restricted to this organ. In this form, the endometrium is largely replaced by a layer of tuberculous granulation tissue and little of the original structure may be found. Caseation and ulceration of the endometrium are usually accompanied by a profuse purulent discharge, at times with bleeding. If the ulcerative or proliferative process should occlude the internal os, the result is a pyometra. Lastly, it may occur as small isolated lesions, few in number, and confined to the endometrium.

The cases in the present series conformed to the third form (Fig. 1) which is also Sutherland's (1943) classification type III. As Bamforth (1950) states, there is no evidence, on clinical examination, that these small isolated lesions, few in number and confined to the endometrium, are associated with tuberculosis of the tubes or other parts of the female genital tract. In the type of endometrial tuberculosis which is encountered unexpectedly the lesions are small, infrequent and formative. They consist of small collections of endothelial cells with or without giant cells. A small central area of caseation may be present but is more often absent. The endothelial cells may be surrounded by a zone of lymphocytes. Sometimes small aggregates of such lesions may be found. In a few cases, there

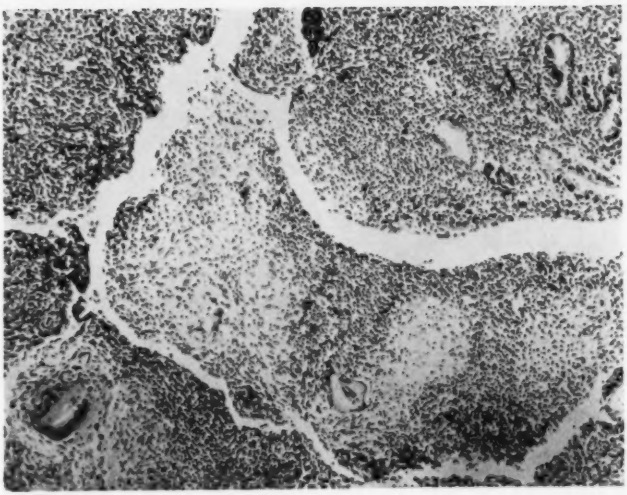

FIG. 1

Post-menopausal endometrial tuberculosis. ×90.

is a more general infiltration of the stroma with lymphocytes and plasma cells. The tubercles are chiefly found in the more superficial part of the endometrium but some may be situated more deeply.

According to Bamforth, there is no doubt about the tuberculous nature of the condition. It is not a non-specific reaction resembling tuberculosis but tuberculosis itself. Most authorities agree that, although there is no clinical evidence that the Fallopian tubes are involved, nevertheless, a sub-clinical tuberculosis of the tubes is also present. Jameson (1935) suggests that the endometrium is constantly re-infected from the tuberculous lesions in the tube. Sharman (1947), however, found that in 3 patients on whom removal of both tubes had been performed, the operation failed to cure the endometrial infection.

Confusion in histological interpretation may arise when lymphocytes are seen in the endometrium. The dangers and shortcomings in the diagnosis of tuberculosis by histology have been emphasized (McDonald and Weed, 1951; Sutherland, 1950) and many investigators (Rich, 1951) are agreed that the diagnosis can only be confirmed by finding the *Myco. tuberculosis*. However, the results of guinea-pig inoculation are fallible (Russell *et al.*, 1951) because the small quantity of endometrium available may not contain living organisms. Furthermore, differential staining of fixed specimens often fails to disclose the presence of *Myco. tuberculosis*. Sutherland (1960) has given up differential staining and is inclined now to accept histological evidence.

In the present series, menstruation had ceased anywhere from 1 to 18 years and yet histological evidence of the disease is clearly present. Since the curettings were inevitably scanty at this stage, it is doubtful if sufficient material could have been obtained for guinea-pig inoculation and, for the reasons already given, the results of this and differential staining would be inconclusive.

The significance of well-defined focal collections of round cells in the endometrium is still controversial. More often than not they belong to a non-specific inflammatory reaction or are of uncertain origin and appear to have no special significance. Every now and then they are the only findings in a case which later proves to be tuberculous (Russell *et al.*, 1951). No lesions of this nature were noted in the post-menopausal endometria. According to Bamforth's (1950) criteria, the diagnosis of the 9 cases of the series is clear-cut from the characteristic histological appearances which they present.

It is appreciated, in the grosser form of tuberculous involvement, that differentiation from other post-menopausal endometrial conditions is sometimes extremely difficult. Wharton (1947) points out how apparent it is that the pathological picture of tuberculous endometritis could readily be confused with endometrial carcinoma. The tuberculous vegetations, proliferating granulation tissue growth from papillary excrescences, ulceration and necrosis demand careful microscopic study before cancer can be ruled out. The symptoms, also, are confusing as endometrial tuberculosis has occurred in elderly women, the only symptoms being leucorrhoea and bleeding. Post-menopausal endometrial tuberculosis can, of course, co-exist with carcinoma of the genital tract. Case 8 showed an epithelioma of the vaginal vault.

Haines (1952) warns that adenomyosis of the uterus, complicated by tuberculosis, may simulate carcinoma of the body of the uterus. Even with regard to senile endometritis, which is so often superimposed on post-menopausal atrophy, Novak and Novak (1958) describe the endometrium as thin and heavily infiltrated with round and plasma cells. Patches of squamous metaplasia may be seen replacing the normal columnar epithelium. Ulceration of the surface is common and a frequent cause of post-menopausal bleeding which must be distinguished from that due to adenocarcinoma.

Summary

The clinical and pathological findings in 9 cases of post-menopausal endometrial tuberculosis are described and discussed together with a review of previous reports.

In conclusion, I would like to thank Dr. A.

Sharman and Dr. A. M. Sutherland for their advice and criticism in the preparation of this study and Mr. Pearston for the photomicrograph.

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DECIDUOSIS PERITONEI IN PREGNANCY

Report of Two Cases Respectively Simulating Carcinoma and Tuberculosis

BY

DONAL O'SULLIVAN, M.A.O.
Registrar

AND

CHARLES K. HEFFERNAN, M.R.C.P.I., D.Path.
Consultant Pathologist
Queen's Park Hospital, Blackburn

MICROSCOPIC subperitoneal deposits of ectopic decidua are common in pregnancy. Geipel (1916) found an incidence of 90 per cent, Harbitz (1936) 85 per cent. Gross deciduosis peritonei, however, as pointed out by Shaw (1927) is rare. Two such cases are reported.

Case 1

Mrs. A.G., an unbooked primigravida aged 34 years, was admitted when 34-weeks pregnant to Queen's Park Hospital on the 31st January, 1958, as an emergency ante-partum haemorrhage. At 18 weeks she had an episode of mild vaginal bleeding which subsided spontaneously. Thereafter the pregnancy proceeded uneventfully until the morning of the day of admission when suddenly and painlessly some large blood clots were passed *per vaginam*. She had been married for 3 years and anxious throughout to have a baby. There was no serious medical or surgical illness noted in her past history. Examination revealed a rather obese woman who looked her age. The baby was alive and presented as a vertex, high and free, in a uterus enlarged to the size of a 34-weeks pregnancy. A speculum examination revealed a minimal erosion affecting the posterior lip of the cervix. The blood pressure was 140/90 mm. Hg. The urine was free of protein, sugar and acetone. A haemoglobin estimation was 83 per cent (Haldane), blood group "O" Rh. positive, Kahn test negative. Placentogram findings outruled an anterior placenta praevia but were otherwise equivocal. A regime of expectant treatment was instituted. Bed rest in hospital and phenobarbitone gr. ½ t.d.s. was prescribed. Two pints of whole compatible blood were kept standing by.

Subsequently she continued to have recurrent small painless losses. At 36 weeks, on the 17th February, 1958, a large painless sudden loss occurred. On the same day a lower segment Caesarean section was performed and a live baby weighing 4 pounds 11 ounces was uneventfully delivered. A left antero-lateral placenta praevia encroaching on the internal os was confirmed.

The uterine surface, pelvic peritoneum and greater omentum were studded with raised greyish-white granular plaques; each of which was on an average about the size of a split pea. A gross diagnosis of carcinoma, probably chorionic in type, was made and a biopsy taken.

Microscopically in the sectioned specimen there were submesothelial collections of decidual cells. These were large polygonal cells, many with protoplasmic protrusions and with eosinophilic cytoplasm surrounding a large pale vesicular nucleus. The cells were arranged in a mosaic pattern and collected into tubercle-like formations. Scanty acute and chronic inflammatory cells were present at a few points at the periphery of these collections. The appearances were those of deciduosis peritonei.

The post-operative period was morbid. Recurrent vomiting and varying degrees of abdominal distension over the first seven days warranted gastric suction and the administration of intravenous fluids. Bowel sounds, however, were satisfactory throughout. A course of penicillin and streptomycin was given intramuscularly after a growth of *Escherichia coli* was isolated from a catheter specimen of urine. Further investigations: Faeces—no shigella,

salmonella or *Staphylococcus pyogenes* isolated. Haemoglobin (Haldane) 65 per cent, colour index 1·3, W.B.C. 12,500, polymorphs 84 per cent, lymphocytes 10 per cent, monocytes 6 per cent. Marrow puncture—megalopoiesis excluded; normoblastic erythropoiesis confirmed. Blood urea 40 mg. per cent. Serum calcium 10·2 mg. per cent. Repeat serum electrolyte estimations were all within limits of normality. A Hogben pregnancy test on 28th February, 1958 was negative.

On the 16th day a course of intravenous iron (Ferrivenin) was commenced and a total of 40 ml. (800 mg. elemental iron) was given. She was discharged home with her baby on the 44th day. Examination on discharge revealed satisfactory involution of the uterus though some nodules were palpable in the pouch of Douglas. The haemoglobin was 92 per cent. On follow-up visits in June and October, 1958 she was found to be fit and well. No local gynaecological abnormality was found on either occasion.

Case 2

Mrs. S.H., an unbooked primigravida, aged 34 years, was transferred from a nursing home to Queen's Park Hospital at 4.00 a.m. on the 14th September, 1958, as a case of uterine inertia. She was at term (40 weeks) and had been in labour for 38 hours. There was a history of 13-years infertility and in 1955 a D. and C. and ovarian cystectomy were performed. Examination on admission revealed her to be in a good state of health. Physical proportions were normal. Hydration was satisfactory and there was no gross anaemia or oedema. A single foetus presented as a vertex R.O.A., engaged. The foetal heart tones and rate were normal. Palpably adequate pains were occurring every seven minutes. The cervix was two-fingers dilated, well taken up and closely applied to the head. Clear liquor was draining. The pelvic bony outlet was adequate. Blood pressure was 130/80 mm. Hg. The urine was free of protein, sugar and acetone. Haemoglobin (Haldane), 75 per cent. Blood group, "A" Rh. positive. Kahn, negative.

A provisional diagnosis of primary uterine inertia was made. Omnipon gr. ½ and scopolamine gr. 1/150 was injected intramuscularly with good sedative effect. Six hours after admission, as the dilatation of cervix despite adequate pains had only advanced to three fingers, it was decided to deliver her forthwith by Caesarean section. A lower segment operation was performed without difficulty. A live baby weighing 8 pounds 3 ounces was delivered.

At operation the surface of the uterus, the broad ligament and vesico-uterine peritoneum were found studded with raised greyish-white tubercles, each 2–3 millimetres (approximately) in diameter. No adhesions were present. A tentative diagnosis of tuberculosis of the peritoneum was made and a biopsy taken. The specimen microscopically revealed submesothelial collections of decidual cells. The appearances were similar to those in Case 1. A diagnosis of deciduosis peritonei was made. Mother and baby progressed satisfactorily but the puerperium was morbid. *Staph. pyogenes* and a proteus group organism were isolated from the upper vagina and *Streptococcus faecalis* from a catheter specimen of urine. All were sensitive to chloramphenicol which was prescribed in an oral dosage of 250 g. 6-hourly for 5 days. The pyrexia, however, did not subside until a necrotic portion of retained membrane was spontaneously evacuated vaginally. On the 14th day as a haemoglobin (Haldane) estimation was found to be 60 per cent a transfusion of two pints of packed cells was given. Subsequently progress was uneventful and she was discharged home fit with baby on the 29th day. Later at a routine follow-up visit she was found fit and healthy.

Discussion

Ectopic decidua of pregnancy was first described by Schmorl (1897) as incidentally found on the posterior aspect of the uterus and the adjacent peritoneum. The term ectopic decidua was coined by Taussig (1906) to describe its extra-mucosal locations. Novak and Novak (1958) list the following sites of ectopic decidua: cervix, vagina, ovary, posterior surface of the uterus, anterior peritoneal surface of the uterus, anterior surface of rectum, floor of cul-de-sac, omentum, appendix, islands of adenomyosis, bands of adhesions, ovarian cyst and peritoneum of small intestine. Further sites mentioned are the Fallopian tubes (Shaw, 1927), mesosigmoid and subdiaphragmatic peritoneum (Harbitz, 1936), lymphatic glands (Russell, 1945), caecum (Bogle, 1946), renal pelvis (Bettinger, 1947) and lungs (Lattes *et al.*, 1956).

Rarely an ectopic decidual reaction may be so gross and vascular as to cause significant complications. In the cervix and/or vaginal vault it can cause vaginal bleeding and macroscopically

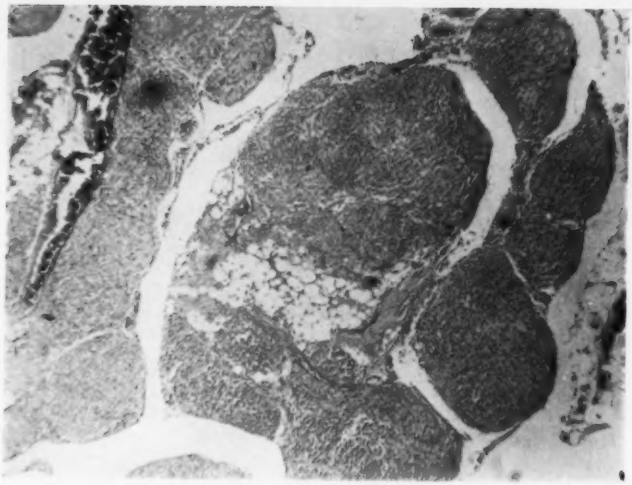

FIG. 1

Multiple groups of decidual cells in omentum. Case 1. Haematoxylin and eosin. ×25.

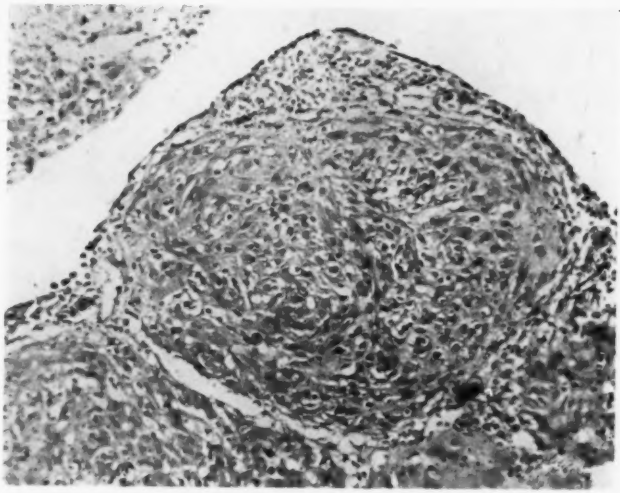

FIG. 2

Photomicrograph showing the submesothelial position of a collection of decidual cells. Case 2. Haematoxylin and eosin. ×75.

simulate carcinoma (Hennessy, 1943; Klein and Domeier, 1946; Lapan, 1949; Bowles and Tilden, 1951; Mathie, 1957). Konwer (1929) reported a case at term of fatal haemoperitoneum resulting from haemorrhagic decidual excrescences at the posterior surface of the uterus. Melody (1950) describes a case of massive haemoperitoneum at term due to deciduosis of the omentum. Kanevskaya and Poz (1959) report a similar case of haemoperitoneum at 32 weeks that survived following a Caesarean hysterectomy. Deciduosis of the vermiform appendix simulating acute appendicitis has been reported by Hirchberg (1905), Reis and Sinykin (1940), Nordlander (1946) and Horvath (1953). Bogle (1946) reports a case of caecal deciduosis at 8 weeks simulating acute appendicitis. A case of haematuria at 4 months resulting from decidual masses in the renal pelvis and warranting nephrectomy is described by Bettinger (1947). Three cases of pulmonary ectopic decidua of pregnancy are on record (Park, 1954; Lattes *et al.*, 1956; Hartz, 1956). In the case of Lattes *et al.*, lobectomy was performed as the lesion from its radiological appearance was thought to be carcinoma of the lung.

The formation of ectopic decidua in pregnancy is essentially a response to progesterone elaborated by the corpus luteum and trophoblast. The characteristic reaction is a metaplastic one, whereby certain stromal cells undergo epithelioid morphological changes. If glandular components are present, it suggests that the tissue affected was originally an area of endometriosis or else that embolisms of the gestational endometrium had occurred. In the latter respect, it is of interest to note that the pulmonary and lymphatic node decidua reported had both had glandular elements. In deciduosis peritonei on the other hand as exemplified in Cases 1 and 2 glandular components are absent.

The undifferentiated subcoelomic mesenchymal cells are thought to be the progenitors of the definitive mesenchymal cells which include the stromal cells of the endometrium. Harbitz (1936) relates the more common occurrence of decidua around the pouch of Douglas to the increased local concentration of progesterone in the peritoneal secretions.

But it is puzzling to dwell on the cause of the rare gross decidual reaction. Meyer (1913) stressed the role of healed low-grade and pre-existing inflammation, especially that associated with the formation of adhesions in the sensitization of tissues to the decidual response. Loeb (1908) produced deciduomas in guinea-pigs by traumatizing the uterus in the progestational phase. Unterberger (1921) confirmed Loeb's work in rabbits. Shelesnyak (1957) induced a decidual reaction in the pseudo-pregnant rat by injecting histamine intravascularly and intraperitoneally. Von Latzka (1937) found the incidence of decidual change much commoner in cervical polyps than in cervical stroma.

Summary

Two cases of gross ectopic decidua of the peritoneum in pregnancy are reported, with respective pitfalls of macroscopic diagnosis. Both were elderly primigravidae and both had a history of infertility. The sites and clinical significance of ectopic decidua are reviewed. The pathogenesis is discussed.

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ISAAC BAKER BROWN, ESQ.

(*See Appendix D*)

CLITORIDECTOMY—THE DISASTROUS DOWNFALL OF ISAAC BAKER BROWN, F.R.C.S. (1867)

BY

J. B. FLEMING, M.A., M.D., M.A.O., F.R.C.P.I., F.R.C.O.G.
Professor of Midwifery and Gynaecology
University of Dublin

Gynaecologist
Adelaide Hospital, Dublin

THE following passage by Lawson Tait (1883) was found to be so full of mystery that it stimulated an investigation to be made into the circumstances which surrounded the downfall of Baker Brown:

> . . . and to this able but most unfortunate surgeon (Baker Brown) I unhesitatingly award the position of having achieved the second great advance in abdominal surgery. He began to operate in 1851, and his career ended in 1867. He established the short incision, the intraperitoneal method of dealing with the pedicle, the use of the actual cautery for its treatment, and the complete closure of the abdominal wound. Between May, 1865 and September, 1867 (that is to say during the time he employed the cautery) he performed forty operations with four deaths, or a mortality of ten per cent.* During the same period, Mr. Spencer Wells operated one hundred and one times with twenty-six deaths; or a mortality of slightly over twenty-five per cent. Verily ovariotomy would have had a very different history during the last fourteen years if Mr. Baker Brown had not fallen a victim to his own folly, or to professional jealousy—for opinions differ very much as to the cause of his death. His methods, again, were in many respects faulty, and have since been immensely improved upon; but I give these details of the result of his practice because here again a most unfair attempt has been made to deprive a man of the credit he has deserved; and, however much Mr. Baker Brown's actions in other respects are to be deplored, and however much he may or may not have deserved his sudden and disastrous downfall, he does deserve to rank second in order of English ovariotomists.

This abridged account of his career is taken from the obituary notice in the *Lancet* for 8th February, 1873:

> ISAAC BAKER BROWN, F.R.C.S. (1812–1873)
>
> One of the ablest and most inventive of English surgeons has just died in Mr. Isaac Baker Brown. The deceased gentleman was born in Essex at Colne Engame† on the 8th of June 1812. He was of honourable parentage, his father being a country gentleman in the neighbourhood, and his mother the daughter of the Rev. James Boyce, celebrated as the master of the Bluecoat School when Samuel Taylor Coleridge and Charles Lamb were pupils. In due time he was entered as a student at Guy's Hospital where he was distinguished in the classes and gained the Astley Cooper prize for Anatomy. He took the diploma of the Royal College of Surgeons in 1834 and in the same year the Licentiateship of the Apothecaries' Hall; fourteen years thereafter he became a Fellow of the College by examination . . . Ovarian dropsy could, he convinced himself, be radically cured only by ovariotomy and accordingly he became an enthusiastic vindicator of the operation . . . This operation he therefore performed, and though unsuccessful with his first three operations, he did not hesitate, in 1852, to operate in the fourth, though the patient was his own sister. That lady is, we are gratified to state, still alive and the mother of several children.
>
> Mr. Baker Brown took an active part in the founding of St. Mary's Hospital,‡ and was appointed at its

* See Appendix A.

† In the *British Medical Journal* report "Engame" is given as "Enguine". See Appendix D.

‡ *British Medical Journal*, 1873, **1**, 158: "About this time (1848) Brown took a very active part in the founding of St. Mary's Hospital, the first meeting being held in his dining-room. At the foundation festival of the Hospital his health was proposed by the Chairman, Prince George of Cambridge, as 'founder of St. Mary's Hospital'." See Appendix B.

commencement, surgeon and accoucheur, a post never refilled since his vacating it in 1858. The London Surgical Home shortly after owed its foundation to him . . . In 1854 appeared his work on *Surgical Diseases of Women*, which has reached a third edition. This work established his celebrity as an operator at once bold, ingenious, and successful, and of itself will ensure his memory. His operating theatre was one of the most attractive to the professional visitor in all London—admiration being invariably invoked by his brilliant dexterity and the power he displayed in the use of his left hand when operating on the female perineum . . . In cases of prolapsus uteri, vesico- and recto-vaginal fistulae, and fibrous tumours of the uterus he was a master, while his favourite operation of ovariotomy owes to him (acting on a hint from Mr. Clay of Birmingham (*sic*)) the reatment of the pedicle by actual cautery.* Failure he never hesitated—as he could easily afford—to confess.

In 1861 he was visited by the French surgeon, Nélaton, who was for some days an inmate of his house. In the presence of his distinguished guest Mr. Baker Brown performed three ovariotomies in succession one afternoon, and M. Nélaton also witnessed his performance in two other cases, and took note of several patients in course of recovering after the operation. On his return to Paris, M. Nélaton gave a clinical lecture on what he had seen, with the result of introducing ovariotomy to the favourable notice of the profession in France.

In 1865, Mr. Baker Brown, then at the zenith of his reputation, was elected President of the Medical Society of London, and in the following year he published his remarks on "The Curability of some Forms of Insanity, Epilepsy, and Hysteria". In this work he set forth his operation of clitoridectomy, which was, we believe, honestly devised as a legitimate resource of surgery.

Shortly after this began the controversy between him and the Obstetrical Society, with the origin of which our readers are already familiar. After the dissolution of his connection with that body (1867) his practice declined, in spite of repeated endeavours to win it back. He was shortly afterwards the subject of successive paralytic seizures, which shattered his already broken health, and were probably aggravated by his having involved himself in a lawsuit with the *Lancet*, in respect of some remarks made by us purely on public grounds, and from which action he was advised to withdraw.

For well-nigh a year he had been in a helpless state, when on Saturday, the 1st February (1873) he was seized with shiverings and headache, symptoms which were soon followed by unconsciousness, and on the morning of the 3rd February he expired, in the sixty-first year of his age.

A detailed description of the post-mortem findings is then given followed by:

The proximate cause of death was apoplexy, in which the congestion, undoubtedly caused by the sudden fall in temperature, terminated.

Mr. Brown was twice married. By his second wife, who survives him, he leaves three children. His young son is a candidate for the foundation of Epsom College, and we hope that, in consequence of his father's services to surgery, and the active part he took in the promotion of professional charities, the candidature will be actively supported.

Let us follow the sequence of events which led to the fall of Baker Brown from his seemingly secure and respected position as a world-famous London gynaecologist. Was the barrage of criticism from his colleagues, which brought him low, justifiable retribution for his conceit, ostentation, and folly? And so to the evidence:

On 20th January, 1866, an editorial in the *British Medical Journal* quoted the *Standard* on "An Admirable Institute—The London Surgical Home".† The editor wrote:‡

. . . We doubt whether the profession will approve of the way in which this particular institution is brought before the public. . . . A superfluous amount of self-laudation is not always a real recommendation.

He then extracted from the same paper this paragraph:

Mr. Baker Brown, F.R.C.S., the founder of the Home, has not only brought to bear upon these cases ordinary and known surgical treatment, but he has actually succeeded in accomplishing with success operations never before performed in England; in one class of cases at least, never, we believe, previously done anywhere.

Further on the editor continued to report Baker Brown's statement that:

I said I thought we had discovered a mode of curing a class of cases hitherto perfectly incurable—I mean cases of epilepsy, sometimes including insanity and hysteria.

Two days later Brown replied to this charge in a letter to the editor (27th January, p. 108) claiming that the article in the *Standard* was written by a distinguished member of the Press connected with that paper, to show his gratitude to the institution for the care of his wife and that the article was not seen by anyone connected with the Home until it appeared in the paper.

* *British Medical Journal*, 1866, **2**, 231. At the 34th Annual General Meeting of the British Medical Association held at Chester, Mr. Brown gave details of thirteen cases of ovariotomy in which he had used the actual cautery in the treatment of the pedicle. In the discussion, Mr. Meade (Bradford) thought that the originator of the method must have taken his idea from the common operation of spaying pigs. Mr. Brown replied that Mr. Meade was quite right as to the plan having been taken from the spaying of sows, and he readily admitted his obligation to veterinary surgeons for the hint.

† See Appendix C.

‡ See Appendix E.

He also stated that the report was published by the committee for circulation, and was in the hands of all governors and friends of the institution. But the editor would have none of this and implied that Mr. Brown was quibbling, for he commented:

> We do not see that the fact of the extracts being made from a report in any way removes their objectionable character. On the contrary, it shews that they have been deliberately circulated, and are not the words of an after-dinner speech.
>
> Mr. Brown and all the medical officers must have seen the report before it was issued, and the extracts we made from the paper were the words of the report itself and of Mr. I. B. Brown.

From this acrimonious exchange it is obvious that Brown had deeply offended the sensibilities of the editor of the powerful *British Medical Journal*, even though the causes which produced this first editorial outburst remain unknown. However, nothing more was heard for several months.

In March, 1866, a slim red volume, with its author's name and title inscribed in clear gold lettering, was brought before the public. This was Baker Brown on *The Curability of certain forms of Insanity, Epilepsy, Catalepsy, and Hysteria in Females*, published by Robert Hardwicke, London. This small book inspired a scathing three-page review from the *British Medical Journal* (1866, **1**, 438) which serves as a pattern of the many charges which were eventually brought against the eminent and successful Mr. Brown. In brief, Brown's thesis was that nervous affections complicating diseases of the female genitalia were the direct result of "peripheral excitement of the pudic nerve" or masturbation. This excitement, Brown maintained, gave rise to disease which could be divided into eight stages—the eighth stage being arrived at, by gradations, more or less distinct, directly from number one. These eight stages were:

1. Hysteria.
2. Spinal irritation.
3. Epileptoid fits or hysterical epilepsy.
4. Cataleptic fits.
5. Epileptic fits.
6. Idiocy.
7. Mania.
8. Death.

To appreciate the hostility of the review fully it would be necessary to study it in detail, but its length does not allow of this. It began:

> We do not propose to attempt a criticism of the operation recommended in Mr. Baker Brown's book; for we confess that it is beyond our knowledge. Mr. Brown proposes a cure for "epilepsy etc.", in females, which is entirely new to us. We have heard of cases of epilepsy in which the testicles have been removed by way of cure; but of excision of the clitoris and nymphae as a cure of that disease, etc., in females, we know nothing except what we learn from Mr. Brown's book. Indeed, we are greatly surprised to read in the opening lines of it these words: "I do not wish it for one moment to be understood that I claim any originality in the surgical treatment herein described." Surely the credit of this operation belongs solely and wholly to Mr. Brown. In what other work, medical or surgical, is excision of the clitoris, etc., recommended as a cure for epilepsy, etc.? That the treatment is original, moreover, is shown by the fact that Mr. Brown himself, throughout his book, speaks of it as "my operation".
>
> Mr. Brown seems desirous of throwing the praise of it on Dr. Brown-Séquard, to whom the work is dedicated. The perusal of Dr. Brown-Séquard's Lectures, Mr. Brown says, first led him to think of "peripheral nervous excitement" as a cause of diseases—led him, in fact, to the conclusion that "nervous affections complicating diseases of the female genitals depended on peripheral excitement of the pudic nerve".
>
> Thus enlightened by physiological experiment, Mr. Brown proceeded to put his conclusion to the test, "by removing the cause of excitement; viz., the clitoris and nymphae". This operation, he now says, he has again and again performed; and the results are such as to convince him, "that all unprejudiced men must adopt, more or less, the practice which I have carried out".
>
> Mr. Brown then describes the symptoms of "the disease". "The patient becomes restless and excited, or melancholy and retiring, listless, and indifferent to the social influences of domestic life. She will even be fanciful in her food, sometimes even express a distaste for it, and apparently (as her friends will say) live upon nothing. She will always be ailing, and complaining of different affections. At first, perhaps, dyspepsia and sickness will be observed; then pain in the head and down the spine; pain, more or less constant, in the lower part of the back, or on either side of the lumbar region. There will be wasting of the face and muscles generally; the skin sometimes dry and harsh, at other times cold and clammy. The pupil will be sometimes contracted, but generally much dilated. This latter symptom, together with a hard cord-like pulse and a constantly moist palm, are, my son informs me, considered by Mr. Moore, Colonial Surgeon of South Australia, pathognomonic of the condition."
>
> Mr. Brown never operates before puberty. Under chloroform, "the clitoris is freely excised with scissors or knife—I always prefer scissors".

Section by section the harsh criticism continued until the last three paragraphs which we reproduce in full:

We have not space to discuss Mr. Brown's theory of "peripheral excitation". We do not consider it well founded in physiology or pathology; and we doubt if Dr. Brown-Séquard would accept it as a satisfactory exposition of his views on the subject. But we can afford to pass by a theory of a diseased state, if we only get a cure for it. And we trust that the further experience of the profession may confirm the statement that excision of the clitoris is capable of curing any of the forms of catalepsy, epilepsy, or insanity.

Mr. Brown will not be surprised that the profession should ask for wider information on the subject. While admitting that his cases show the operation may be of value in certain forms of nervous disease, we cannot help suspecting that Mr. Brown has considerably exaggerated its value. Indeed, anyone who has read the last Annual Report of the London Surgical Home, will not have failed to note that a regrettable spirit of exaggeration attaches generally to the doings of its medical officers.

We feel bound also to observe, that a serious medical work on the subject of Female Masturbation should bear on its outward *facies* none of those characters which belong to the class of works which lie upon drawing-room tables. There surely was no necessity that this little book should not only bear its title with the author's name on the back, but also have a sort of title-page in gilt letters also with the author's name spread over its side. Mr. Brown is not responsible for the doings of his publisher, but still he will, we hope, in future have the objectionable feature to which we allude removed.

To these unkind words Mr. Brown replied not at all.

In the "Medical News" column of the same *British Medical Journal* (p. 456) a short paragraph entitled "Spiritual Advice" appeared:

The *Church Times* thus speaks of Mr. Baker Brown's new book:

We desire to call the attention of the clergy especially to a little book, which will enable them to suggest a remedy for some of the most distressing cases of illness which they frequently discover amongst their parishioners. Epileptic affections have long been considered usually incurable. Mr. Baker Brown, F.R.C.S., the eminent surgeon, has discovered and applied with great success, at the London Surgical Home for Gentlewomen and elsewhere, a surgical remedy for certain forms of epilepsy and kindred diseases. He has published through Mr. Hardwicke a little volume of cases, which prove incontestably the success of the treatment, and which the clergy will be doing a service, especially to their poorer parishioners, by bringing under the notice of medical men, any of whom can, if possessed of ordinary surgical skill, perform the operation with but slight assistance.

The next issue (p. 478) printed a long letter on "Mr. Baker Brown's Operation":

Sir,

In common with, I know, many of my professional brethren, I am most pleased that you have reviewed as you have done Mr. I. B. Brown's late publication and the subject to which it really relates.

There is one question which must occur to everyone, and I put it with all professional propriety: What is the value, *in toro nuptiali*, of a woman on whom "the operation as usual" has been performed? I have heard of bachelors fighting shy of young ladies who are known to have consulted a certain celebrated physician who insists in a "digital exploration" in every case of illness, but this! . . . . . .

I rejoice to read your strictures also, mild as they are, on the "Report of the London Surgical Home" sent, be it remarked, to half the nobility in the kingdom . . .

I had already been astounded by the notice in the *Church Times*, which you quote at page 456. Fancy some innocent curate going about recommending his easy little operation for "distressing cases of illness".

I am, etc.,
A Provincial F.R.C.P.

In the issue of the *British Medical Journal* for 12th May (p. 509), in the section "To Correspondents", a reference was made to Mr. I. B. Brown's operation:

Dr. Brown-Séquard, we understand, does not at all agree with Mr. I. B. Brown as to the value of excision of the clitoris. Mr. Brown's work is dedicated to Dr. Brown-Séquard; and it might be inferred from the dedication and other remarks in it, that Dr. Brown-Séquard had given his tacit assent to the theory and practice of Mr. Brown in his cure of "peripheral excitement of the pudic nerve". To Mr. Brown alone, therefore, must attach all the honours on which he founds it. Dr. Brown-Séquard, as we are told, declines any reflected rays of credit, such as Mr. Brown desires to throw upon him, out of the pages of his work on Female Masturbation and its Cure. The only rival we know of to Mr. Brown is a Dr. Braun of Vienna, who has lately published papers on the Cure of Masturbation in the Female by Excision of the Clitoris. But then, Dr. Braun of Vienna is certainly later in the field than Mr. Brown of London.

After this the letters appeared in the *Journal* fairly regularly, and on 19th May, Thos. Littleton, F.R.C.S., wrote to say that the operation had been performed by Aëtius and that caution should deter the profession from inflicting such a serious mutilation. In conclusion he advised Mr. Brown that, on the strength of the adage "What is sauce for the goose is sauce for the gander" and to be consistent, he should extend the advantages of the operation to both sexes.

The next attack on Brown was made in a leading article in the *British Medical Journal* for 2nd June, 1866 at page 579. Entitled "A Proposed Testimonial", the editorial opened:

A printed circular is in course of distribution amongst members of the medical profession, which states that, on the 16th of February, at a meeting held in the Hanover Square Rooms (J. Propert Esq., in the chair), the following resolution was unanimously passed. "That this meeting, having regard to the long-continued zeal, skill, and boldness with which Mr. Baker Brown has laboured in the face of many obstacles for the advancement of obstetric surgery, and fully recognizing the great improvements he has achieved therein, spreading the fame of his operations throughout the world, in every part of which his merits have been fully acknowledged, is of opinion that a testimonial should be presented to him, as a mark of personal esteem and the general appreciation of his eminently practical services as a surgeon and operator; and the meeting pledges itself to use its best exertions, individually and collectively, to carry out this object."

The document does not state who was present to compose the unanimity, nor even who proposed the unanimously carried resolution. On the face of the thing, as it present stands, Mr. Propert is the proposer and seconder, and, in fact, the embodiment of the meeting . . . Now, surely, it is not usual or regular to issue resolutions without giving the names of the resolvers. Surely also the profession ought to know who called the meeting, and under what auspices it was held. There is positively no proof that, at the getting up of this testimonial-proposal, anyone else was present besides Mr. Propert and the door-keeper.

We are, we suppose, to conclude from the proceeding that Mr. Propert considers, either that Mr. I. B. Brown's services have not been hitherto sufficiently appreciated by the profession and public, or that they are so greatly appreciated as to require testimonialising. As Mr. I. B. Brown's claim to a testimonial must mainly be founded on the services which he has rendered to science at the Surgical Home, we will give our readers an account of his merits, as told by himself and his friends in the last Annual Report of the London Surgical Home.

The editor, methodically and without mercy, tore the report apart and submitted the "noble master" and the Home itself to a gruelling of which these extracts are typical:

Self-laudation and the exchange of compliments run bravely through the Report, and were carried on mainly, if not entirely, by gentlemen officially connected with the "Home" . . . The saying, that a man is not a prophet in his own country, is assuredly not verified in the present case.

In conclusion the Editor wrote:

The friends of Mr. I. B. Brown have, therefore, perhaps done well in thus eliciting an expression of opinion on the part of the profession outside the somewhat narrow limits of the staff of the Surgical Home. At all events, the profession now has an opportunity of testimonialising their appreciation of Mr. I. B. Brown's services in the cause of medical science.

At long last the silence is broken by Brown in the *British Medical Journal* for 2nd June (p. 593), when he feebly replied to Littleton's letter:

Sir,

So long as letters with reference to me and the operation of clitoridectomy were anonymous, I did not think them worth answering. The letter, however, of Mr Littleton, in your issue of May 19th, is of a different class; and, in reply to it, I beg leave to make a few remarks . . . (These deal chiefly with the historical aspect of the operation.)

I shall be happy to give any additional information to any gentleman actuated by an honest desire to know the truth; but I do not feel disposed to enter into a wordy warfare with those who, professedly seeking for light, hide themselves under the mantle of an anonymous contribution.

I am, Sir, etc.,
I. Baker Brown

A three-month respite followed until the *British Medical Journal* for 8th September printed this at page 296:

Testimonial to Baker Brown Esq., F.R.C.S.

The object of this testimonial being to give both the profession and the public generally an opportunity of testifying their opinion and appreciation of the eminent services which Mr. Baker Brown has rendered as a surgeon and operator, it is considered that this will be better shown by the large number of subscribers than by the amount of their individual subscriptions; and that all who desire it may have an opportunity of expressing their appreciation of those services, contributions will be received, however small. All friends who intend to subscribe, are earnestly requested to communicate at once to Dr. Holt Dunn, the Hon. Sec., 109 Hereford Road, Westbourne Park, W.

The Editor commented:

This notice is followed by a list of subscribers; amongst whom are included several givers of 2s. 6d. and 1s. up to £5 5s. The subscriptions here published seem to amount to about £150.

Up to 24th November, 1866, the letters in the *British Medical Journal* on the subject of "Mr. Baker Brown's Operation" tended to be short, sarcastic, and unsigned. After this date there was a change to lengthy pronouncements from the senior men on "Clitoridectomy" and all seemed

anxious and eager to involve Brown more and more deeply in a controversy. The first of these was from Dr. Charles West (p. 585)* who requested the Editor to publish a statement, "in the belief that his former position as a teacher in the largest medical school in London not only justified his doing so, but rendered it an act of duty".

Under eight headings West stated his opinions categorically. The first five of these gave his general ideas on the frequency and injurious effects of the vice in the female. The last three are quoted in full as they resembled the charges which were eventually to be brought against Brown.

6. Whilst I believe the removal of the clitoris in cases of hysteria, epilepsy, insanity, and other nervous diseases of women to be a proceeding theoretically based on erroneous physiology, and practically followed by no such results as to warrant its frequent performance, I regard it as completely unjustifiable when done for the alleged relief of dysuria or of painful defaecation, for the cure of amenorrhoea, or for the mitigation of the symptoms of uterine misplacement or disease.

7. I consider that public attempts to excite the attention of non-medical persons, and especially of women, to the subject of self-abuse in the female sex are likely to injure society, and to bring discredit on the medical profession. I think that such attempts are the more objectionable when associated with a reference to some peculiar mode of treatment and alleged cure practised by one individual.

8. I believe that few members of the medical profession will dissent from the opinion that the removal of the clitoris without the cognisance of the patient and her friends, without full explanation of the proceeding, and without the concurrence of some other practitioner selected by the patient or her friends, is in the highest degree improper, and calls for the strongest reprobation.

The next event of importance was the meeting of the Obstetrical Society of London, held on 3rd December, when Dr. T. Hawkes Tanner read a paper on "Excision of the clitoris as a cure for hysteria, etc", which was followed by a discussion in which Baker Brown participated. The leader in the *British Medical Journal* of 15th December (p. 664) demonstrated the mood of the time as can be seen from these extracts:

The subject of clitoridectomy was brought before the Obstetrical Society of London at its last meeting, in a paper read by Dr. Tanner; and it is much to be regretted that the discussion of the question was made an occasion for the display of a good deal of personal feeling . . . With scarcely an exception, the opinions expressed were decidedly adverse to the proceeding of clitoridectomy . . . It is urged against Mr. Brown that he is so possessed with the idea of the universality of the habit of self-abuse, and its power of producing innumerable evils, that he resorts to the operation with lamentable frequency. As a consequence of this, practitioners are constantly meeting with patients who are not only unrelieved by this treatment, but are even left worse, to say nothing of the stigma which has been cast upon their moral character . . .

We would venture to make a suggestion to the Obstetrical Society, which, we think, offers a means of settling it in a way which will be satisfactory. Let a Committee be appointed to investigate the matter; let at least twenty cases of twelve months' standing be carefully observed, and their history both before and after the operation be thoroughly inquired into; then let a report be drawn up, giving the result of the Committee's experience . . . The letter which we print today from Dr. West expresses, not one whit too strongly, the disgust which reasonable and thinking men feel at the public discussion, before mixed audiences, of sexual abuses. It is a dirty subject, and one with which only a strong sense of duty can induce professional men to meddle; and then it needs to be handled with an absolute purity of speech, thought, and expression, and, as far as possible, in strictly technical language.

Between 24th November, 1866 and 16th March, 1867 the controversy raged in long letters in the *British Medical Journal*, but because of their length it is not possible to condense them. Ten such, all antagonistic to Brown, were written by Charles West (3), Robert Greenhalgh (2) and one each from James Paget, Holmes Coote, Henry Maudsley, Forbes Winslow, and John Locking. During this time Brown replied at length in his own defence on three occasions while his sole ally was Robert D. Harling who wrote twice in his support.

The issue of the *British Medical Journal* for 22nd December printed a short notice in the section called "The Week" (p. 702) which followed the leading articles:

A Hint to the Lunacy Commissioners

We would direct the attention of the Lunacy Commissioners to the paragraph in *The Times* which gives an account of Mr. Baker Brown's "Surgical Home". It seems that: "A peculiar feature of the Home is that, in addition to the ordinary maladies which come under the head of surgical diseases, women are received who are of unsound mind, provided that their infirmities are not hereditary or of long duration previous to their application for admission. In it the great experiment is being made, for the first time, of endeavouring to cure mental diseases by surgical operations."

* See Appendix E.

Unless a house be licensed for the reception of persons of unsound mind, and unless intimation of their admission be given, the law is transgressed; and, under such circumstances, the offenders are usually prosecuted, even when no "great surgical experiment" has been performed upon the lunatic. It is worthy of note that, whereas Mr. Brown has stated that in many cases Dr. Maudsley attributes insanity to the cause which Mr. Brown declares to be so general, so fertile in insanity, Dr. Maudsley writes to us today flatly to contradict the statement, as Dr. West flatly denies the acts which Mr. Brown attributes to him. Dr. Maudsley said precisely the reverse. He has never known insanity to be traceable to this cause; and in the one case of insanity in which Mr. Brown performed "his operation", the patient was not one whit the better.

The *British Medical Journal* for 19th January, 1867 (p. 61) followed with a leader:

THE OBSTETRICAL SOCIETY

We proposed several weeks since that the Society . . . should institute a searching inquiry. This was with a view to avoid the paper warfare which we saw impending, and of which it was not difficult to foresee that the result could not be satisfactory . . . We think that, before proceeding to appoint a Committee on Clitoridectomy, the Council ought to consider the moral and professional aspects of the charges which have been made, and the circumstances which have been brought to light. If terrorism have been used to frighten patients into submission, where need for operation there was none; if serious operations have been performed upon patients without their knowledge and consent, and without the knowledge and consent of their friends; if one operation have in any case been suggested, in order that another might be performed, the Council, before committing itself to any other inquiry, should make an investigation into these circumstances, and should determine what its course of action should be. The Obstetrical Society owes a duty to "science"; it owes another duty to professional honour and public morality. Unless it fulfil the latter duty in all its respects, it will be weakened, if not powerless to influence medical opinion by its verdicts generally.

At the request of the Lunacy Commissioners, the *British Medical Journal* for 26th January (p. 94) published the whole correspondence which passed between that body and the Surgical Home for Women.

Jan. 3rd, 1867.

Sir,

I am directed to transmit for your perusal the enclosed copy of a paragraph which appeared in *The Times* newspaper of the 15th ultimo; and to inform you that the House Surgeon of the London Surgical Home, having attended a meeting of this Board on Monday last to explain that paragraph, then substantially admitted to the Commissioners present the reception into the Home of females of unsound mind.

The Commissioners will now be pleased to hear from your self, as Senior Surgeon of the Home, whether there is any and what mistake in the paragraph, or on the part of the House Surgeon, as to the objects of the Home; and, if any mistake has arisen, whether you have taken, or immediately intend to take, any and what steps to disabuse the public mind upon the subject of this apparent violation of the Lunacy Law.

I am, Sir, your obedient servant,
Charles Palmer Phillips, Secretary.

(The paragraph in question reads as follows: A peculiar feature of the Home is, that, in addition to the ordinary maladies which come under the head of surgical diseases, women are received who are of unsound mind, provided that their infirmities are not hereditary or of long duration previous to their application for admission. In it the great experiment is being made for the first time of endeavouring to cure mental diseases by surgical operations.)

Mr. Baker Brown promptly replied from 136 Harley Street on 5th January:

Sir,

In answer to your communication dated the 3rd inst., I beg to state that the article in *The Times* newspaper to which you refer, was written by a gentleman, a perfect stranger to me, who came on the part of *The Times* newspaper, was shown over the Home, and supplied with all the papers by the Secretary; and I never saw the article until it appeared in print the next morning. I was very much vexed by the mistake therein, and instantly took steps to ensure correction as I thought would be sufficient. I have been daily waiting to see my hopes realised, and am now most willing to take any steps the Commissioners may advise to disabuse the public mind upon the subject of any violation of the Lunacy Law.

I shall be very happy to wait upon the Commissioners to offer any further explanation, if they think it necessary.

I remain, etc.,
I. B. Brown

To which the Commissioners replied on 8th January:

Sir,

The Commissioners, observing with pleasure your sense of the gravity of the mistake in *The Times*' article of the 15th ultimo, upon the London Surgical Home, direct me to acknowledge receipt of your letter of the 5th inst., and at once to obtain from yourself, as Senior Surgeon of that institution, a plain and direct contradiction of its being open for the reception of females of unsound mind. The Commissioners doubt not that, in possession of such an authoritative contradiction, they will be able themselves to procure for it that necessary publicity which you have failed hitherto to get.

I am, etc., Secretary.

Two days later Brown replied:

Sir.

I have no hesitation at once in stating, as Senior Surgeon and founder of the London Surgical Home, that the institution is not open for the reception of females of unsound mind, and in no papers or advertisements issued or published with authority has it ever been stated so. During last year, one patient, a servant of ——, was taken in as suffering from hysteria. I immediately discovered that she was of unsound mind, and, as quickly as possible, had her removed to Hanwell Asylum.

I am, etc.,
I. B. Brown.

Editorial comment in the *British Medical Journal:*

**** Mr. Baker Brown must feel highly favoured that a special reporter should have been despatched from Printing House Square to describe his institution. We presume, however, that the statement made in the report was furnished to that gentleman by someone officially connected with the Home. The profession will take note of Mr. Brown's announcement, that no patient of unsound mind has been cured of the disorder by clitoridectomy, in the Surgical Home. It was understood that such cures were the striking proofs of the efficacy of that procedure.

Like a terrier the Editor kept snarling at his victim for, in a sub-leader of 2nd February (p. 119) this can be read:

Surgery for Lunatics

In the painful and disgusting case of Hancock *v.* Peaty, the advocate, Dr. Spinks, stated that the unfortunate lunatic had been placed under the care of Mr. Baker Brown, who, unknown to her husband, had performed a most cruel, he might say barbarous, operation upon her.

As this is one of the great experiments for the cure of mental diseases by surgical operation, to which *The Times*, on unknown authority, alluded, and which Mr. Baker Brown so promptly confused his house-surgeon by repudiating, so far as his Home is concerned, when interrogated by the Lunacy Commissioners, the statement of Dr. Spinks is not without importance . . . We have the best authority for stating that the above statements have engaged the attention of the Lunacy Commissioners.

Again, one week later, another sub-leader was printed (p. 144):

Surgery for Lunatics

In a letter of date January 10th, 1867, Mr. I. B. Brown wrote as follows to the Secretary of the Commissioners in Lunacy (see *British Medical Journal*, January 26th):

"I have no hesitation at once in stating, as Senior Surgeon and founder of the London Surgical Home, that the institution is not open for the reception of females of unsound mind, and in no papers or advertisements issued with authority has it ever been stated so."

Perhaps Mr. I. B. Brown may think it necessary, when his attention is called to the point, to reconcile this unhesitating assertion with the following statements, which are to be found in a work written and published by him in 1866. His book bears the title, *On the Curability of Certain Forms of Insanity, Etc.*; and he offers, as a proof of the authenticity of the cases in it, that "the majority of them were taken from the records of the London Surgical Home".

The Editor then described some details of five cases extracted from the book:

Case 47. Acute hysterical mania;
Case 43. Incipient suicidal mania;
Case 42. Epileptic fits, with complete idiocy;
Case 41. Epileptic fits, with dementia;
Case 39. Epilepsy, with dementia;

all of which were admitted to the London Surgical Home for treatment, and concluded:

If Mr. Brown has so soon forgotten his reported cases, probably it has also slipped his memory that only last year the papers were sounding a great note of triumph, blown to the benefit of the Surgical Home, and to the tune that Mr. Brown had at that institution discovered or perfected a new cure for insanity in some of its shapes.

The next week, 16th February, another sub-leader appeared in the *British Medical Journal* (p. 179):

The Council of the Obstetrical Society

The Council of the Obstetrical Society are summoned to a special meeting this evening "to consider two letters from Mr. Baker Brown". Mr. Brown had addressed a letter to the Council, offering to submit twenty cases of clitoridectomy to investigation. This he announced freely in the press at the time. He has since, we are informed, withdrawn the offer. The proceedings of the Council will be watched with considerable interest.

While these events were taking place, two letters appeared in the *Journal* which should be read in full. On 9th February, the Secretary of the London Surgical Home wrote to the Editor (p. 154):

Sir,

I am directed by the two Senior Surgeons, Mr. Baker Brown and Mr. Philip Harper, to state that, *solely* in deference to the opinion of the medical press on clitoridectomy, they have determined not to perform the operation in this institution, pending professional inquiry into its validity as a scientific and justifiable operation. An early insertion of this note in your *Journal* will oblige.

Yours etc.,
Wollaston F. Pym,
Secretary

London Surgical Home,
Stanley Terrace, Notting Hill, W.

Its sequel showed that Brown did not keep his word as can be seen from this extract (*British Medical Journal*, 16th March, p. 301):

Mr. Baker Brown.

The following letter has been forwarded to us for publication.

To the Board of Governors of
the London Surgical Home.
17 Connaught Square,
March 12th., 1867.

Gentlemen,

On the 9th and 13th of February, there appeared in the medical journals a letter from your Secretary, to the effect that he was directed by Mr. Baker Brown and Mr. Harper to state that the operation of clitoridectomy would not again be performed at the London Surgical Home, pending professional inquiry, etc.

On the 21st of February, a patient in Room No. 11 at the Home was placed under chloroform and the said operation practically carried out by Mr. Baker Brown, although not performed in his usual manner.* I am not aware that any consultation took place to decide on operating in this case; nor do I think that any member of the staff was aware of Mr. Brown's intention to operate.

Considering this act as a decided breach of faith with the profession (all the members of the staff being more or less implicated, but having no control in the matter), I came to a decision on the instant that, at the earliest proper opportunity, I must resign my appointment as one of the visiting surgeons; and I now beg leave most respectfully to tender my resignation.

I remain, gentlemen,
Your most obedient servant,
John Locking, M.D.

The protracted wordy battle in the *Journal* came to a head quite suddenly with the printing on 9th March (p. 271) of a letter from the Obstetrical Society to Brown:

To I. Baker Brown Esq. 53 Berners Street,
February 27th, 1867.

Sir,

We are directed by the Council of the Obstetrical Society to forward you a copy of the following Resolution, passed at Special Meetings of the Council held on the 15th and 25th inst., for the purpose of considering two letters addressed to the President and Council by Mr. I. Baker Brown.

"That in the opinion of this Council the published matters in relation to the performance of clitoridectomy by Mr. I. Baker Brown, justify the Council in recommending the Society to put in force against him Law IV, Section II, which provides for the expulsion of a Fellow."

We are, Sir, your obedient servants,
G. W. P. Murray, M.D.
Henry Gervis, M.D. Hon. Secs.

23rd March brought another leader from the Editor of the *British Medical Journal* (p. 328), entitled "The Obstetrical Society":

The Council of the Obstetrical Society have, according to the resolution of the Society, issued to the Fellows the "extracts from the published matter" on which they base their recommendation that Mr. Baker Brown be removed from the Society. They are very numerous, and constitute a good-sized pamphlet, consisting of extracts from the letters and articles which have already appeared in this JOURNAL, and some of them in the other medical papers. Those passages are selected especially which bear upon professional conduct, rather than those which have a surgical bearing. The document is properly marked confidential and we refrain from any comments upon it.†

A full attendance of Fellows is expected at the meeting at which the resolution of the Council will be considered and put to the vote; and, for the convenience of the Fellows, the voting will be by papers at a large table. The President will, we trust, be supported by all the Fellows in preserving order on this painful occasion, and in restraining injudicious ebullitions of feeling on either side.

Before the special meeting was held to decide the fate of Brown, the Editor had a last say in a leader printed in the *Journal* on 30th March (p. 361):

The Obstetrical Society

On Wednesday next, the Obstetrical Society will meet to receive and vote upon the formal proposition of the Council in respect of Mr. Baker Brown. The subject has been fully discussed of late, not only in the profession but beyond it, and in the clubs; attention having been especially drawn to Mr. Baker Brown by a card circulated by a London silversmith, and by newspaper paragraphs giving a copy of an inscription on a piece of testimonial plate setting forth the great skill of Mr. Brown, and his professional success in this department of practice. This, in connexion (sic) with the impending verdict of the Society upon his professional conduct, has drawn an unusual amount of attention to the subject. We trust that the discussion will be conducted with prudence and dignity, and that the honour of the Society and the

* February 21st. On examining the clitoris, labia, etc., this day, the surfaces were of a pale or white colour, the result of friction or masturbation. The caput clitoridis was seized in a pair of vulsellum forceps and removed by the actual cautery.

† The *Lancet*, April 6th (p. 427): After the "trial" the *Lancet* printed "a comparative extract of the charges made against Mr. Brown, as put forth by the Council of the Obstetrical Society, and the replies thereto, arranged side by side, with the view of placing the profession in possession of the facts, which as yet have only been made known to the Fellows of the Obstetrical Society".

highest interests of the profession at large will be secured by the final result—whatever it may be. It is time that discussions, in many respects unpleasant, on so painful a topic should cease. The Council of the Society have done what they conceive to be their duty; and they are entitled to the thanks of the profession for the moral courage which they have shewn in acting up to their opinions. It is now for the Society to take that course which may seem best to support the common object of the members. The Society has to pronounce an ethical judgment; and the profession is deeply interested in its verdict.

The monthly meeting of the Obstetrical Society, held on 3rd April, 1867, pursuant to notice, was convened for the purpose of considering the recommendation of its Council in reference to the conduct of Mr. I. Baker Brown, one of the Fellows of the Society.

Although the meeting was timed for eight o'clock, the members started to arrive shortly after seven and long before the appointed time all the seats in the large room, which had been arranged for the convenience of the Fellows, were full as well as the standing room. In addition to the London group, some fifty practitioners from all parts of the country attended "to hear, to judge, and to vote upon the issue presented to them". The Chair was taken by the President, Dr. J. Hall Davis, who, on opening the proceedings, said:

We have met here this evening specially, in pursuance of the notice which I read at the last meeting of the Society, to consider and to vote upon a resolution which was notified at that meeting . . . I shall mention that the vote will be taken at nine o'clock this evening. The resolution will be proposed by Mr. Seymour Haden, and will be seconded by Dr. Barnes; then the reply of Mr. Brown will be heard, and any other remarks from other Fellows of the Society. Shortly before the time of the ballot Dr. Barnes will reply upon the case. The ballot will be taken in the next room, and it must be distinctly understood that those gentlemen who do not vote must be considered as voting for Mr. Brown. The vote will be according to the rule to which I referred.

Then the Honorary Secretary, Dr. Murray said:

If, on a ballot taking place (for the removal of a Fellow), two-thirds of the Fellows present shall vote for the removal, the President shall declare the Fellow in question removed accordingly.

At this point Dr. Routh spoke:

Allow me to ask one question before you proceed. (Cries of "order", "no, no", and "chair".)

The President:

I now call upon Mr. Seymour Haden to propose the resolution.

Dr. Routh:

I wish to put one question. (Cries of "order", "chair", "no, no", "sit down", and great confusion.)

From the start of the meeting the business proceeded until midnight. The verbatim report in the *British Medical Journal* (p. 395) occupies almost fifteen pages and as it cannot be condensed it should be read in full, for otherwise the hostility of the meeting towards the unfortunate Brown cannot be appreciated. The proposer of the resolution, before proceeding with what he had to say, read it:

That, in pursuance of the resolution of the Council notified to the Society's General Meeting, March 6th., Mr. Isaac Baker Brown be and is removed from the Fellowship of the Obstetrical Society of London. . . . The motives which have induced me to bring it forward may be included perhaps in what I might call the growing insensibility on the part of the profession to the inroads of quackery, and its consequent decline in public opinion. These are the reasons which have brought me here tonight.

Having referred to quackery in some of its forms, the opener continued:

This form consists (if I understand it) in the pretended cure of real disease by means which have no foundation in philosophy or in fact, and which in addition have more or less of a secret, unpublishable, compromising character. I think that is a fair definition of the form of quackery which we are called this evening to consider. . . . Having made these specious promises (of cure), what wonder that some poor weak woman, or even that some weaker man should take a wife or daughter to the Home and place her under the promoter of the scheme! It is sure to happen; and what occurs there is simply this. The patient is put under chloroform; the inducement of course has been enlarged upon; the operation is so very trifling: it is a mere nothing perhaps, except the cutting of a pile or the excision of a nerve. The husband remains downstairs. The patient is taken up and placed under chloroform, and her clitoris cut out before recovering from the anaesthetic. Down comes the promoter of the scheme to the expectant victim below; invites him to write a cheque for 100 or 200 guineas, or whatever it may be, before he leaves the house. Now, if he object to this, which he is very likely to do, I do not say that he is informed, but at all events he is made to feel this: "Your daughter" or "Your wife", as the case may be, "has undergone a disgraceful mutilation, because she has been given to disgraceful practices; if you can afford to tell your friends this, and to tell the man who is to

marry her that she has had her clitoris cut out, and that for disgraceful practices, well and good; but if you cannot afford to tell them this, I think you had better pay the money and say no more about it." (Cries of "No, no", "Oh, oh", and great uproar) . . . I do not mean to be unfair, or to go one step beyond what the circumstances warrant. But of that fact I am positively certain, that there are many women who dare not speak of this; and that Mr. Brown knows it well when he cuts out their clitorides. (Cheers) . . . Very well, then, Mr. Brown has distinctly asserted that he cures insanity, in many of its forms, by means of this operation. But that does not prevent him writing a letter to Mr. Phillips, the Secretary of the Lunacy Commissioners, to declare that, in no papers or advertisements, issued or published, has it ever been stated that females of unsound mind had been operated upon, or admitted even into the Home. (Hear, hear.) Either he has cured these people or the whole thing is a sham. . . . I choose to believe that when he wrote to the Lunacy Commissioners to say that no case of insanity had ever been operated upon, or even admitted into the Home—I choose to believe that in that single letter Mr. Brown states the truth, and therefore I think that we have convicted him of quackery, and that clitoridectomy is quackery. . . . I entreat you to let no casuistry of Mr. Brown's or indeed of any other speaker, interfere with your healthy understanding of that point (of supporting Brown). You endorse his principles, and you accept his acts if you do not support the Council tonight (Hear, hear), and in future professional honour and truth will be measured by the standard that you have thus deliberately set up.

Seconding the resolution, Dr. Barnes was reviewing other aspects of the charges when suddenly the President spoke:

I wish to remind you that the ballot will commence at nine o'clock for the convenience of those gentlemen living at a distance who may wish to leave the meeting at that hour.

Dr. Barnes:

I will not detain the meeting one minute.

President:

I am reminded by the Secretary that I must give the names of the scrutineers. They will be Dr. Parsons and Dr. Tanner, if they will kindly consent.

Mr. Brown:

But you cannot pretend not to allow me to make a single observation to that; you cannot pretend to go to the vote, without hearing my reply to them.

President:

Your reply will be heard directly.

Dr. Barnes then continued his seconding of the resolution during which the President announced:

The scrutineers will retire in order to examine the ballotting papers.

Mr. Brown:

But, Mr. President, may I not be allowed to say a word in reply after the speeches from the mover and seconder, which have lasted an hour?

President:

It is not so. I said at the commencement that Mr. Brown would have a reply, and that Dr. Barnes would have the final reply to the whole case.

Secretary:

I may mention that the ballot-box will not close until every speaker has spoken. It is only for the convenience of those gentlemen who wish to go into the country, and who have made up their minds one way or the other.

Dr. Barnes concluded his speech with these words:

If we have any regard for the honour of the profession and for the expression of public opinion; if we desire to have the Society held in the slightest respect, we must act in this matter. It is impossible that those, who have devoted most time and most attention to the affairs of the Society, can possibly go on, if this imputation of appearing to sanction proceedings of this kind rests upon them. There is no doubt of this fact, that the Society is used by Mr. Brown in encouraging the public to think that this is a professional and legitimate matter. (Hear, hear.) The profession will judge by the voice of the Society in this matter. We have put ourselves forward as the exponents of professional opinion in this matter, and as we pronounce, so will be the judgment of the public; and, I say, that we cannot, unless we are prepared to bow our heads in shame and degradation, go on as we have been doing, without speaking on the subject.

At this stage, Mr. Baker Brown rose to make what proved to be a fruitless attempt to preserve his professional status. Subjected to constant interruption and "ironical cheers", he was forced to make several appeals to the chair to maintain order while he was speaking. Though he failed, he did his utmost to vindicate his position and to answer the charges, relying on his fame as an ovariotomist. We can quote only certain passages from his long defence:

. . . The whole of this hinges upon the neglect of the Council in investigating the subject of clitoridectomy as scientific men. Instead of examining the subject, which I

challenged them to do again and again, they have neglected it, and tried to get rid of it by expelling me . . . I hope you will maintain order, Sir, when I am speaking . . Mr. Haden has scandalised the Home in the most shameful way possible. I say that the way in which he has described the proceedings there is untrue from beginning to end. (Mr. Haden: "No, no!" Great confusion.) . . . I never went down and demanded a fee from a husband or father. There were no fees demanded at the Home.*

. . . In that home there have been, according to the entry book, 3,417 entries of medical men who have visited it in the last seven years since its formation; I do not say that they are the signatures of 3,417 individual men, for many gentlemen have been there again and again, much oftener than they state; but if I did the thing in secret, if I had practised quackery, why should I invite all the profession to come and see me? Why should they come without an invitation? From the north, the south, the east, and the west; from the Antipodes, from Australia, from Sydney, from Melbourne, and from every state in America: why have they come?

When loud laughter, hisses and groans greeted Brown's statement that clitoridectomy was neither more nor less than circumcision, he continued:

I have heard the same noises before in this room. I have heard the same noises before within ten years, when a man dared to get up and say that the speculum ought to be used. Why, look how my friend, Dr. Henry Bennet, was met in this room because he dared to use the speculum in examining a woman's uterus. How did they treat him? Did not they condemn him and write him down? (Cries of "No, no!") They did; and yet my friend Dr. Bennet's practice has proved to be a standing practice in the profession.

When Brown started to talk about the subject of ovariotomy, because of his eminent position as an expert in that field, the following exchange occurred:

President:

This is not the question.

Mr. Brown:

Not the question?

President:

We shall be here all night if we are to go into these matters.

Mr. Haden:

It is no answer to the charges.

* See Appendix C.

Because of continuous interruptions a Dr. Savage felt compelled to rise and to say:

Speaking on behalf of some gentlemen who are sitting round me, I may state that we desire that Mr. Brown should have an uninterrupted hearing. There were no interruptions made to the previous speakers, and I think that we ought to hear what Mr. Brown has to say.

And at once, Mr. Oldham:

I think it will be a wise thing on the part of the Society to allow Mr. Brown to speak without interruption (Hear, hear); and we shall finish what we have to do tonight far better. It will be better both for Mr. Brown and ourselves if we listen to his statements.

Mr. Brown continued:

I am glad, at last, I have an opportunity of being heard quietly. I need not tell you I stand here in a very painful position, and it is not kind to interrupt me; it is not manly to interrupt me, for no man can talk when he is interrupted so repeatedly as I have been tonight . . . I have performed the operation because I believed it to be a justifiable operation. I have done it to the best of my judgment, and in a way which I considered professional . . . Why, gentlemen, I have in my pocket a letter from a gentleman who was written to by a member of the Council to ask him to come up and vote; and his remark was that the case must be a very bad one if he wants whippers-in. It is well known, that every effort has been made by the Council to bring voters up; and they now have put forth a threat, that, if the motion is not carried, the Council will resign . . . You may pass a vote condemning me tonight. I do not think you will; I do not think that there are so many against me in the Society. But if you do, I tell you frankly I shall not consider it a stigma. And, as it will apply to myself, I am surely the best judge of what I consider a stigma, because I feel that I have not been treated fairly tonight.

Then Mr. Robins, Dr. Savage, and Dr. Routh spoke on Brown's behalf and when Dr. Barnes rose to sum up the discussion he was met with loud cries of "Vote, vote" and "Divide, divide".

President:

I will call upon Dr. Barnes to reply, if the meeting wishes it. ("No, no", "Divide, divide".)

Dr. Barnes:

I will merely call to mind the fact that no one of the main charges has been touched upon by Mr. Baker Brown or his friends. He expressly avoided the question I put to him. (Cries of "Enough, enough", "Divide, divide" and applause.)

The ballot was then taken. At about ten minutes to twelve the scrutineers entered the room which was full, although many country

members and others had been compelled to leave. As Dr. Braxton Hicks, Dr. Murray, Dr. Tanner, and Dr. Parsons advanced up the room, there was a dead silence. The President, with evident emotion, said:

The scrutineers have handed me the following statement; "We, the undersigned, scrutineers of the ballot for the removal of Mr. I. Baker Brown from the Obstetrical Society of London, do hereby state the following as the result.

	Votes
For the removal of Mr. Brown	194
Against the removal	38
Non-voters	5
	237

Thus, it appears that the motion of the Council for the removal of Mr. Brown from the Obstetrical Society is carried by thirty-six votes above the required majority of two-thirds.

T. H. Tanner,
Edward Parsons, Secretaries
J. Braxton Hicks, Vice-President
G. C. P. Murray, Hon. Secretary

After Brown had been arraigned before the Obstetrical Society and expelled, both the *Lancet* and the *British Medical Journal* devoted the leading article to a comment on the decision. The *Lancet* (1867, **1**, 420) wrote:

So long as the question was still under discussion whether it was expedient for the Obstetrical Society of London to remove from its body a member who was asserted to be unworthy of its Fellowship, we thought it our duty to refrain from influencing the votes of the Fellows in a matter which, however powerfully it might interest the profession at large, was for the time being in their hands, and could only be dealt with safely by their own considerations.

. . . For it must be remembered that the verdict which was pronounced on Wednesday evening bore no direct relation to the utility or uselessness of a particular operation. That is a question which may or may not one day receive its final solution. The point which has lately been at issue was whether a Fellow of the Obstetrical Society was proved to have so far departed from the rules of professional honour as to render his retention in the Society an outrage upon the feelings of the Fellows, and a discredit to the profession of which they are members.

The Society has expressed its conclusion, and this with an unanimity which precludes all doubt as to the necessity of the unusual step which has been taken. We may pronounce it as decided that the medical profession, speaking through a section of its body, utterly discountenances and repudiates the proceedings which have made one of their number notorious. It protests indignantly against the performance of a dreadful operation upon married women without the consent of their husbands, and upon married and unmarried women without their own knowledge of the nature of the operation. It denounces the behaviour of a surgeon who deliberately insults and compromises a fellow-practitioner by performing in his presence a mutilation as to which his sanction is unasked. It scorns the miserable quibbling by which a palpable want of veracity is sought to be defended.

This short, restrained and succinct editorial admirably summarized the episode and can be compared with that in the *British Medical Journal* (1867, **1**, 387) which had attacked the unfortunate Brown right from the start. This editorial ran as follows:

It is seldom that any professional association is called upon to pronounce a verdict on a case of so profoundedly painful a character as that which was finally submitted for the judgment of the Obstetrical Society on Wednesday night. On this occasion, they had to debate upon a proposition to remove a well-known member from the Society, upon the ground of grave ethical faults. The incident is one which, in the history of the profession in the metropolis, can find no parallel; and we believe that all were fully impressed with its gravity. The Society had assembled to decide whether the Fellow accused of conduct which, if rightly laid to his door, could not be too severely reprehended, was guilty of that conduct; and whether, if guilty, he should be removed. It was a function such as that which the General Medical Council* is invested by law in respect to the whole profession, and one which is inherent in the constitution of every voluntary association.

The matters to be brought under the notice of the Fellows had no character of novelty. They were avowedly not only published matters, but twice published and twice answered. It will not be necessary to weary our readers with the thrice-told tale . . . There was much heat and a strong tinge of personal feeling in some parts of the debate; but this was provoked chiefly by the reprehensible line of defence which Mr. Brown pursued. His accusations and groundless charges of hatred, malice, and unfairness, were no doubt trying to men who, as Mr. Haden observed, had throughout leant to mercy. His speech produced a painful impression upon those who listened to it. He spoke as though he had not yet had time to consider charges which had already been twice published, and with which every one else is as much wearied as disgusted. He pronounced his own condemnation . . . So severe a punishment as this has not fallen upon any man holding a respectable position in our profession in the memory of any of us. It is impossible not to feel pity and deep regret for the man who thus suffers—pity for one who has brought upon

* The activities of Baker Brown did not result in his name being erased by the Council nor was there any reference to him in the Council's Minutes of the period.

himself so cruel a blow from hands which are so rarely raised except to uphold a brother—regret that abilities of a high order, and practical skill of a most undeniable kind, have not been controlled by a higher sense of ethical propriety. The fault has been great; the punishment is severe. Let us hope that the future may cause the past to be condoned.

When Brown had been expelled from the Obstetrical Society, he immediately tendered his resignation to the Medical Society of London, of which he had been a recent President. The question of his resignation was duly debated and Dr. Routh, who had supported him in the discussion in the Obstetrical Society, moved a successful amendment to the effect that his resignation should be deferred. The *British Medical Journal* for 13th April (p. 428) commented:

It is not impossible that the matter will be ultimately referred to a general meeting, and that thus an attempt will be made to constitute the Medical Society of London a sort of court of appeal from the Obstetrical Society. This is, we think, greatly to be deprecated. It may injure the Society very seriously; it cannot benefit Mr. Brown.

However, the *British Medical Journal* for 27th April (p. 487) reported:

A special meeting of the Medical Society of London was held on Wednesday evening last, when the resignation of Mr. I. B. Brown of the Fellowship of the Society was "unanimously accepted".

Three weeks after the number which reported the expulsion of Brown, the *British Medical Journal*, in a leader (27th April, p. 489), recorded:

Acting the part of impartial annalists, we feel bound to record the following, which we take from the columns of the *Standard* of April 18th.

THE BAKER BROWN TESTIMONIAL

This testimonial was presented yesterday, at the private residence of Mr. Brown. The testimonial is of the value of three hundred guineas, and has been subscribed for by nearly as many persons, either professional admirers or grateful patients of Mr. Brown. It consists of a silver dessert service of six pieces—a centre-piece, plateau, and four fruit stands, *en suite*. The centre-piece has six arms, and a centre-glass for either flowers or fruit; and the crest of Dr. Brown is introduced at the base. The following is the inscription: "Presented to Baker Brown Esq., F.R.C.S. (Examd.), by several of the nobility, gentry, and members of the medical profession, both in this country and abroad, in token of their appreciation of his marked surgical skill and singular success in the treatment of female diseases, March, 1867." The testimonial was manufactured by Mr. Benson, of 25, Bond Street. It was presented, in an appropriate speech, by Mr. Propert, and was gracefully acknowledged by Mr. Brown.

In putting this on record, we fulfil that important part of the duty of the contemporary historian which Tacitus has sketched:

"Precipuum munus annalium reor ne virtutes sileantur, utque pravis dictis factisque, et posteritate et infamiâ metus sit." (The primary function of history is, I believe, that virtues should not be passed over in silence, and that vicious words and deeds should be opposed for fear of future infamy.)

It was ironical that the presentation of the testimonial from his well-wishers should more or less coincide with his expulsion from the Obstetrical Society and his subsequent resignation from the Medical Society of London.

The publicity given to these events brought about his complete ruin and he was reduced to penury. The London Surgical Home continued until 1870 having changed its title and address several times.* Under "Medical News" the *British Medical Journal* for 3rd August, 1867 (p. 78) wrote:

The London Surgical Home

We understand that, Mr. Baker Brown, having forwarded a communication to the Committee of the London Surgical Home, tendering his resignation on the ground that he felt obliged to do so by the state of his health, the Committee met on Tuesday last and accepted the resignation with the customary expressions of regret. It was resolved at the same meeting of the Committee that it would not be expedient to carry on the Surgical Home in its present form, and that it would be necessary, either to remodel the staff and throw open the institution to another committee, or to take other and more decisive steps.

The rest is silence. What befell the man? This question is best answered by quoting in full a letter to the *Lancet* from Forbes Winslow, M.D., and published on 25th January, 1873 (p. 151) shortly before Brown's death.

Sir,

In the early part of last year, an appeal was made to the members of the medical profession on behalf of Mr. Isaac Baker Brown, who was then in great pecuniary difficulties, and suffering from an attack of apparently incurable paralysis. The profession nobly and generously responded to this appeal, and placed at my disposal the handsome sum of £404–10–6. to be expended as I

* See Appendix C.

thought best for Mr. Brown's benefit. I am now desirous of laying before the subscribers an account of the trusteeship with which I was honoured, and to give some particulars as to the expenditure of the money.

In the first instance, it was unavoidably necessary to release Mr. Brown from some pressing liabilities with which he was hampered. This absorbed about £50 of the fund. I afterwards allowed him two guineas a week for his maintenance. After a few weeks, it was thought desirable for him to leave London for the country; and accordingly, at his own request, he resided for some time in an hydropathic establishment at Beulah Spa. This entailed an expenditure of three guineas per week. On his return to London at the end of the summer, I continued to allow him this sum, under the belief that, considering the acute character of his cerebral illness, his life could not be of long duration . . .

I have suggested to Mrs. Brown that the fund should give two guineas per week. To this she has consented . . . There is now a balance in hand of £219–3–10.

Mr. and Mrs. Brown (whom I saw yesterday) are full of gratitude to those friends who so kindly came forward to their relief in the hour of their bitter distress. Personally, I desire to express my sense of the great obligation under which the subscribers have laid me, and to thank them for so liberally assisting me with this work of Christian charity.

I am, etc.,
Forbes Winslow. M.D.

Cavendish Square, January 18th., 1873.

. . . and so, financially supported by the profession, he died on the morning of 3rd February, 1873. The last reference to the story is to be found in a second letter to the *Lancet* by Winslow published on 8th March, 1873 (p. 361):

Sir,

May I trespass once more on your kindness, and be permitted through your Journal to inform the subscribers to "The Baker Brown Fund" that it is proposed that Mrs. Brown be permitted to draw from the balance of the fund (£217–17–10) £2–2–0. weekly, for the support of herself and three young children, respectively aged eight, seven, and five, as well as to aid in the maintenance of a crippled daughter of Mr. Brown's by a former wife.

I beg to acknowledge the receipt of a donation of £5 from "An Old Patient" sent, since Mr. Brown's death, by Dr. Nichol of Denmark Hill.

I am, Sir, your obedient servant,
Forbes Winslow. M.D.

Cavendish Square,
March 3rd., 1873.

These then are the facts of the case. Was he a quack, a showman, a liar, and a fraud? No doubt his success as a bold and courageous operator, which raised him to an important position in the profession at that time, made his more timid rivals extremely jealous. All this glorification of self, in due course, increased his unpopularity to an extent that was manifest in his unsympathetic hearing at the trial. Even on that fateful night, in his conceit, he so lacked the sense of atmosphere that he firmly believed that he had few antagonists. The extent of this error of judgment is reflected in the voting figures. It is a pity that he did not rest content with his unequalled excellence as a gynaecological surgeon of the first rank. By involving himself, however sincerely, with the highly controversial and dangerous subject of clitoridectomy progress in ovariotomy was considerably slowed for some time. However much we may speculate about his character and his shortcomings, he was an acknowledged leader in ovariotomy, and medical men from all over the world travelled to London to see him demonstrate his skill.

Acknowledgments

Professor J. D. H. Widdess, Librarian, Royal College of Surgeons in Ireland, has earned our thanks for providing most of the books and journals used in this investigation. Our thanks are due to Mr. Alan Powditch, House Governor, St. Mary's Hospital, for sending the extracts from the original Board Minutes which are given in Appendix B. Mr. Wade, Librarian, Royal Society of Medicine, helped by producing the drawing of Brown together with the notices of the London Surgical Home which are reproduced in Appendix C. It is a very real pleasure to thank Professor William Doolin, Professor Frank Kane, Professor Miles Phillips, and Dr. R. B. McDowell for their help in the preparation of this paper. We also thank the Editors of the *British Medical Journal* and *Lancet* for permission to quote extracts from their journals.

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1866, Vol. 2: Brown, I. B., p. 675; West, C., p. 676; "James Paget", p. 678; Coote, H., p. 705; Maudsley, H., p. 705; Harling, R. D., p. 706; Winslow, F., p. 706; Brown, I. B.,

p. 706; West, C., p. 728; Greenhalgh, R., p. 729.
1867, Vol. 1: Brown, I. B., p. 18; Harling, R. D., p. 40; Greenhalgh, R., p. 41; Locking, J., p. 301.

Appendix A

In the introduction it was stated that Baker Brown's mortality rate in a series of ovariotomies was 10 per cent, and this figure is repeated often in the literature. We have seen how Brown lied when confronted with the dilemma presented by the letters of the Lunacy Commissioners. Shortly after the *British Medical Journal* had started its campaign against Brown, the following letter appeared in that Journal for 3rd February, 1866 (p. 133):

Mortality after Ovariotomy

Sir,

Mr. Baker Brown has favoured us with his view of the *Standard's* puff of the *Surgical Home*. Perhaps he will also favour us with his view of his own statement about the results of ovariotomy in the Home, compared with the results obtained by Mr. Spencer Wells in the Samaritan Hospital. Mr. Brown says in the last Report circulated among his subscribers, speaking of his success in ovariotomy: "No institution in the world can show a greater amount of success than we can." Now, according to his own statement at page 16 of the wonderful report, and a recent report of Mr. Wells' cases in the Samaritan Hospital, the success in the two institutions is as follows: Home—Cases 51; cures 33; deaths 18; mortality per cent 35. Hospital—Cases 75; cures 54; deaths 21; mortality per cent 28. A "greater amount of success" by seven per cent. seems a pretty conclusive reply to the boast which is scattered broadcast over the country. Only nobody takes the trouble to reply to such things, and so they are believed.

I am, etc.,
Statist.

As there was no reply from Brown to this allegation, it seems likely that Statist's remarks were well founded in fact and could not be refuted. It does, however, make one suspect the accuracy of Brown's figures and doubt if his published results were really true. Nevertheless, Lawson Tait wrote in his praise as can be seen in the opening lines of this paper. Dr. T. Keith, in a letter to the *British Medical Journal* for 31st July, 1880 supported all that Tait was to say in 1883.

> . . . Simple experience with the clamp alone did little to diminish this mortality; for, in Mr. Wells' published eight hundred cases, the death rate in the last three hundred was greater than in the previous three hundred. His results by the dropped ligature were even worse—thirty-eight per cent. All over the frightful mortality of one in four continued.
>
> For some time past it has seemed to me that, had Baker Brown lived, the history of this operation since 1864 would have been different. His own method of dealing with the pedicle by the cautery at once lowered the mortality to one-half of that with the clamp, and it was becoming practised in London when illness came to him, and death. The man and his method were quickly forgotten; no one would have the lesson his work gave. All were strangely blind in those days to its value. Should I not rather say, we were all strongly prejudiced? In truth, there is no more startling page in surgical history than that in which his latest results are given. On one page we have almost nothing but failures; on the other, by a simple change in the method of operating, an almost uninterrupted line of successes. During the whole of his professional life he seems to have tried hard to cure ovarian disease. From 1851 to 1864 he made many efforts and tried many ways, all in vain, till he adopted the cautery. His published results show a mortality of less than one in ten in completed cases. I have read somewhere that he lost but four of his last fifty operations . . . Have I not reason, therefore, for saying that, had Mr. Baker Brown lived, the history of ovariotomy since 1864 would have been changed.

The same Dr. Keith had written previously to the *British Medical Journal* on the subject of ovariotomy (19th October, 1878) stating that his success had largely been due to the adoption of the cautery method as well as some other factors. Of the cautery method he had this to say:

> . . . "and to the use of the cautery method in dividing the pedicle, as proposed and practised by the late Mr. Baker Brown. How the lesson given by his last results has been so systematically ignored in London has always been a marvel to me."

It is difficult, if not impossible, to reach any conclusion about the truth and accuracy of the figures when these two opposite views are recorded. For our part, if a choice had to be made, we feel bound to accept the statements of Tait and Keith in assessing the true worth of Brown's contribution and to reject the opinion of the anonymous "Statist".

Appendix B

St. Mary's Hospital

According to the Board Minutes of the Hospital, which have been read by Mr. Alan Powditch, the House Governor, to whom our thanks are due, the original Laws laid down that there should be a Surgeon-Accoucheur, and in 1851 a special Election Committee recommended the appointment of I. Baker Brown, Esq. to that office.

At a meeting of the Governors of St. Mary's Hospital held in the Board Room at 1.30 o'clock on Friday, 21st January, 1859 the following letter was read:

17 late 16, Connaught Square,
Hyde Park, West,
January 21st, 1859.

To the Chairman of the Weekly Board.

Sir,

I have had the honor of holding the appointment of Surgeon-Accoucheur to St. Mary's Hospital for eight

years, and I have endeavoured to fulfil my duties with zeal and punctuality.

I now find my health so seriously affected by these duties, in conjunction with those of my private practice, that I am compelled to resign my appointment as Surgeon-Accoucheur and Lecturer on Midwifery, etc. I have taken this opportunity of doing so, because I believe this is the best time to fill up the vacancy and make the necessary arrangements for the Summer Session of the Medical School. I shall therefore only hold office till my successor is appointed.

I am, Sir,
Your obedient Servant,
I. B. Brown.

It was resolved:

That this Board greatly acknowledging the zealous services of Mr. Baker Brown in advancing the interests of this Hospital from its commencement as well as the great professional ability and kindness to his patients with which he has performed his duties as Surgeon-Accoucheur of this Institution; tenders to him its thanks, and accepts his resignation with regret.

At a meeting of the Board on Friday, 28th January, 1859 it was resolved:

That the office of Surgeon-Accoucheur being vacant the Medical Committee be requested to report to this Board as to the expediency of retaining the office or making such alterations in the laws as its abolition may require.

Subsequently in the Minutes of the Board Meeting held on 11th February, 1859, the following entry appeared:

That with reference to the resolution of the Weekly Board of January 28th relative to the vacant office of Surgeon-Accoucheur, the Surgeons of the Hospital being willing to perform the operations hitherto performed by the Surgeon-Accoucheur, the Committee recommend that the Office of Surgeon-Accoucheur be abolished.

and they also recommended:

That an alteration be made in the Laws in consequence of the recommendation to abolish the office of Surgeon-Accoucheur.

Appendix C

This institution was founded by Baker Brown in 1858 as "The London Home, for Surgical Diseases of Women, 16, Stanley Terrace, Notting Hill". At this time he was Surgeon-Accoucheur to St. Mary's Hospital from which he resigned in January, 1859. An advertisement in the *London and Provincial Medical Directory* for 1860 stated that it contained twenty beds.

In 1861 the title was changed to "The London Surgical Home for Diseases of Women", the address remaining at "16". The notice in the *Medical Directory* for 1864 showed that the address had been changed to "17 & 18" and that the number of beds had risen to thirty-four.

The most elaborate notice was that in the *Medical Directory* for 1866 which showed that the title had been changed to "The London Surgical Home" with the address of "18, Stanley Terrace, Notting Hill". The size of this insertion showed that the "Home" at this date had reached its zenith for later references became gradually smaller following Brown's expulsion from the Obstetrical Society. As might be expected the entry for 1867 was the same size as that of the previous year (with Wollaston F. Pym as Secretary) for, at the time of the publication of the *Directory*, the storm had not yet broken.

The title was changed yet again in the small notice in the *Medical Directory* for 1868 to "The London Surgical Home, for Diseases and Accidents of Women, 18, Stanley Terrace". The entry for the year 1869 had shrunk even further and the address had changed to "136, Harley Street, near Regent's Park". The *Medical Directory* for 1870 printed the last reference to the title when the address was given as "2, Osnaburgh Place, Regent's Park, N.W.", which was Brown's address until he died in 1873.

The rise and fall of the "Home" over its short career can be readily followed from these notices. Though the institution was advertised after Brown's expulsion in 1867, it is likely that it had little reality until a rapid decline led to its disappearance in 1870. It should be noted that the advertisements stated that "the services of the medical officers are entirely honorary" or "gratuitous", and that "all medical men are admitted to see the practice on Thursdays, at 2 p.m., on application to one of the medical officers at 'The Home' ".

Appendix D

The drawing of Brown has been taken from the *Medical Circular and General Advertiser* 1852, Vol. 1, p. 261. Each issue of the journal at that time published the portrait of a famous medical personality followed by a biographical notice. It so happened that the portraits of Baker Brown and William Chowne became transposed because the original one of Chowne was unsatisfactory and that of Brown was printed to fill the space while another one of Chowne was being prepared. Because of this the drawing of Brown is followed by the biographical notice of Chowne and vice versa. When the copy in the library of the Royal College of Surgeons in Ireland was brought down, it was found that the double page containing the picture of Brown had been forcibly torn out. Was this the act of some hostile reader or did someone merely wish to have a portrait of this notorious character?

The lengthy biographical notice, written when Brown was 40 years old, confirms the important position that he held in the profession at that time. Already he had published 12 important papers most of which dealt with diseases of the ovaries. The notice ends as follows:

It is, moreover, due to Mr. Brown to state, that he was one of the first to advocate the use of, as well as to administer, chloroform in midwifery, and during most obstetrical operations; and an extensive practice in this branch of our art has only served to strengthen the opinions which he holds, on this much vexed and

vexatious subject, in common with Professor Simpson of Edinburgh.

We have thus glanced at what Mr. Brown has done and is still bent on doing for the cause chiefly of obstetrical surgery, whereby he has already raised himself to a distinguished position amongst the leading members of our profession.

(A portrait of this gentleman appeared in No. 14 of this Journal.)

Appendix E

During the Brown affair the editorial chair of the *British Medical Journal* was occupied by two men; William Orlando Markham and Ernest Abraham Hart. The present Editor, Dr. H. A. Clegg, has confirmed that Markham resigned following his appointment as a poor-law inspector (*Brit. med. J.*, 11th August, 1866, p. 163). Dr. Hart was appointed to the post on 22nd November, 1866 (*Brit. med. J.*, 1866, Vol. 2, p. 618).

REPORTS OF SOCIETIES

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

April 1960

A meeting of the North of England Obstetrical and Gynaecological Society was held in Liverpool on the 22nd April, 1960. The President, Professor Jeffcoate, was in the Chair.

Mr. R. M. Corbet described

A Large Fibroid

Large fibroids, in the white races at least, were becoming rare. The patient, aged 38 years, saw her doctor early in December, 1959, but so little did her symptoms trouble her that she did not attend the Preston Royal Infirmary until 14th January, 1960. She had noticed swelling of the abdomen for 2 years and menorrhagia for 1 year.

A large, irregular, immobile abdominal tumour was found. Its upper border disappeared under the ribs, and on vaginal examination a mass filled the pelvis so that the cervix could not be reached. Despite this there was no complaint of dyspareunia.

Before operation her haemoglobin was estimated at 78 per cent, and an excretion pyelogram showed hydronephrotic changes on the right side. Both ureters were dilated and the left ureter was laterally displaced.

At operation, because of some retching when in the lithotomy position, the appearances were those of a patient in the second stage of labour. A catheter could only be passed after relaxation. A large incision was required, and the tumour was seen to be a mass of fibroids covered by large veins. The pelvic tumour was found to be a pedunculated fibroid, and after this had been dislodged with some difficulty, the whole mass was eventrated. The left infundibulo-pelvic, right ovarian and both round ligaments were divided and ligated on both sides because of the enlarged veins. The bladder was displaced upwards and several large vessels required tying when the peritoneum above the bladder was divided. After the bladder had been pushed down the rest of the operation was relatively easy. There was no difficulty in peritonizing the pelvis, blood loss was not excessive and the ureters were not encountered. Recovery was uneventful.

The tumour weighed 6,700 g. (14 pounds 11 ounces). Other examples of large fibroids are:

Operator	Year of Operation	Weight in Pounds
1. Cullen (1907)	1906	89
2. Webster (1903)	1902	87
3. Beacham *et al.* (1947) ..	1942	55
4. Stevens (1925)	1925	47·5
5. Marshall (1924)	1924	47
6. Farmer (1923)	1923	35

References

Beacham, W. D., Holmes, J. A., Beacham, H. T., Mitchell, G. J., Callender, C. G., and Beacham, D. W. (1947): *Amer. J. Obstet. Gynec.*, **53**, 839.

Cullen, T. S. (1907): *J. Amer. med. Ass.*, **48**, 1491.

Farmer, C. (1923): *Kentucky med J.*, **21**, 543.

Marshall, M. Y. (1924): *Kentucky med. J.*, **22**, 253.

Stevens, T. G. (1925): *J. Obstet. Gynaec. Brit. Emp.*, **32**, 729.

Webster, J. C. (1903): *J. Obstet. Gynaec. Brit. Emp.*, **4**, 135.

Discussion

Mr. F. Da Cunha had removed a fibroid weighing 27 pounds. The patient was a single woman of 37 years, and, though the bladder was so distorted that it was opened and later a fistula had to be repaired, she made a satisfactory recovery.

Dr. R. Newton had removed a fibroid weighing 30 pounds. The fibroid was thriving on a huge adventitious blood supply.

Professor C. S. Russell was interested in big fibroids as they present several difficulties in removal. The ureters are often displaced and distorted, so that it is best to divide the broad ligaments in front and work backwards, palpating to find the ureters. When the fibroid is low down the uterus often cannot be removed without first enucleating the fibroid, and often the uterine vessels may themselves be displaced.

Mr. T. B. FitzGerald was interested in the patient's strong disinclination to surgery, and asked what fibroids could be left.

In reply Mr. Corbet issued a word of warning about enucleating a fibroid. This should be left until after the uterine vessels have been tied. Probably if the tumour is the size of a fist it should be removed.

Mr. D. H. Blakey read a paper on

Multiple Retroperitoneal Smooth Muscle Tumours
A Report of Two Cases Treated by X-rays

(This article appears on page 1000 of this issue)

Discussion

The President thanked Mr. Blakey for bringing these cases to the notice of the Society. He mentioned the relationship between ovarian function and growth of the fibroid, but did not think that the effect of oestrogen on tumours in animals could be compared with the activity on uterine myomata. He asked why the effect of the X-rays was thought to be due to the cessation of ovarian function and not a direct action on the tumours.

Mr. T. F. Redman had enucleated a tumour which was said to be sarcomatous, and the patient had remained

well. In another case, after removal of a mass of sarcomatous material, the radiotherapist had advised against X-ray therapy, and the residual tumour was no bigger. He asked if X-ray therapy is effective.

Mr. F. Stabler referred to the second case. The section was very like that of a dysgerminoma, and a dysgerminoma is radio-sensitive.

Mr. R. M. Corbet had not seen a patient with sarcomatous change in a fibroid who came to harm, but sarcoma in the uterus is quickly lethal.

Dr. R. Newton confirmed the last statement. He had known 2 slow growing sarcomata, it being 2 and 7 years before the patients died.

Professor Jeffcoate reminded the Society of an almost identical discussion that had occurred in 1931. Then, sarcoma had been found in a fibroid removed at myomectomy. The opinion of the Society had been to do nothing further. Two years later the patient had a baby, and 2 years after that she died riddled with sarcoma.

In reply Mr. Blakey said only a small dose of X-ray had been used and the beam directed at the ovaries. The tumour sectioned in the 2nd case had been removed from the recto-vaginal septum, and he did not think it was a dysgerminoma.

Mr. E. Parry-Jones read a paper on

THE LYMPHATICS OF THE VULVA

(This article appears on page 919 of this issue)

Discussion

The President: This Society is accustomed to hearing papers of unusual merit and we would like to congratulate Mr. Parry-Jones. It is easy to accept what already has been said and not investigate afresh. Is it not logical to conclude that the fourchette need not be removed if the carcinoma is well forward as all the lymphatics run forwards?

Mr. T. B. FitzGerald mentioned that many authorities maintained the lymphatics crossed, but in none of the pictures was there evidence of contralateral involvement in carcinoma.

Mr. P. Malpas commented on the controversial nature of this work as it could alter the technique in vulvectomy. He remembered the failures with interstitial radium, the dread of wound sepsis and need for primary closure. Because of the few cases any surgeon sees it is necessary to build up a composite picture. The mons, oblique and vertical groin glands are important, but he had never seen spread above Poupart's ligament. An underlying cause in infection is tension in the stitches, and it is necessary to leave at any rate part of the wound open.

Mr. H. Agar thought the extent of the operation must depend on abnormal drainage when the lymphatics are blocked with carcinoma.

Dr. R. Newton observed that some of the bad results are due to the discomfort and hernia formation if Poupart ligament is divided. He removes part of the urethra, and skin grafts are only satisfactory in the young patient.

Mr. R. M. Corbet operated in two stages and did not remove the mons. So far he had had no primary mortality.

In reply Mr. Parry-Jones stressed that he had tried to demonstrate the normal lymphatic drainage, and he had no knowledge of abnormal drainage. This work should not indicate that insufficient operation should be done. It had been possible to close the wound in the last 6 cases, and healing was complete in 2 weeks. The inguinal and femoral nodes must be removed, direct spread might be extensive, but he had not demonstrated lymphatic spread across the midline.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

MAY 1960

A meeting of the North of England Obstetrical and Gynaecological Society was held in Newcastle on the 27th May, 1960. The President, Professor T. N. A. Jeffcoate, was in the Chair.

Mr. Rutherford Morison reported

A CASE OF MYO-HYPERPLASIA ASSOCIATED WITH A BAD OBSTETRIC HISTORY

The patient, aged 25 years, was seen in the 14th week of her second pregnancy, the first having ended in abortion at the 12th week. She was only 5 feet 1 inch tall and weighed 11 stones. The antenatal period was uneventful, but in labour a transverse lie was found. Under anaesthesia a leg was brought down, and labour continued normally until full dilatation of the cervix, when the foetal heart was heard to be irregular. A breech delivery was attempted, but owing to a firm contraction ring round the neck immediate delivery was abandoned. Two hours later a stillborn 4-pound infant was delivered. The puerperium was normal, but the uterus remained the size of a 20-weeks pregnancy even when normal menstruation was resumed.

It was thought that a fibroid must be present and laparotomy was performed 19 days after a period. No fibroid was seen, but the uterus was found to be greatly enlarged due to the thickness of the myometrium. An active corpus luteum was removed. She had no further period, and a Hogben test was positive. After 8-weeks amenorrhoea the uterus was the size of a 22-week pregnancy, but thereafter the discrepancy in the size and period of amenorrhoea became less marked. A transverse lie was corrected, but soon after labour started the foetal heart could not be heard and a stillborn child was delivered.

She attended again at the 24th week of her next pregnancy, Caesarean secton was performed at the 39th week, and a living child weighing 5 pounds 13 ounces was delivered, but died after repeated attacks of cyanosis. The placenta was abnormally large and oedematous. The uterus contained no fibroid, though the upper segment was twice the normal thickness.

In the fifth pregnancy the lie was persistently unstable. At the 38th week of pregnancy the foetal heart became irregular and an emergency Caesarean section was performed. The placenta was again found to be large and oedematous and the uterine wall thick. The uterus remained the size of an 18-week pregnancy when normal menstruation was resumed. Despite cyanotic attacks the 8-pound baby survived. No antibodies were demonstrated, the Wassermann test was negative, the glucose tolerance curve normal, renal function tests within normal limits, but an X-ray showed a flat pelvis.

Discussion

The President wondered if adenomyosis had been considered and if a hysterogram had been done.

Professor J. K. Russell enquired about a biopsy and Mr. P. Malpas considered the condition to be true muscle hypertrophy.

Mr. D. Tacchi read a short paper

Peripheral Vascular Response to Apresoline in Toxaemia of Pregnancy

Toxaemia of pregnancy is associated with a generalized vasospasm of the terminal arterioles, and this spasm can be seen in the retinal and conjunctival vessels. Hypertension may be the protective mechanism to produce an adequate blood supply to vital organs, but it also increases the risk of cerebral haemorrhage and renal damage, and the vasoconstriction present in toxaemia is associated with a reduction in uterine blood flow.

In pregnancy toxaemia a hypotensive drug should relieve peripheral vasoconstriction and increase placental circulation, and of the many preparations Apresoline (1-hydrazinophthalazine hydrochloride) meets these requirements. The conjunctival vessels were studied in 14 hypertensive patients before and after intravenous Apresoline, using a standard Poser slit-lamp the barrel of one of the eyepieces being fitted with a camera.

The conjunctiva was scanned and an easily recognizable area found. Apresoline was injected slowly, the dose varying between 8 and 60 mg.; the blood pressure was checked frequently, and the conjunctiva was photographed 15 and 30 minutes after the completion of the injection.

In each case a reduction in blood pressure was recorded usually after 20 to 40 mg. Apresoline. In 11 patients a change was seen in the conjunctival vascular bed at 15 or 30 minutes after the injection: relief of arteriolar spasm was observed in 4 instances, dilatation of the capillaries in 9 and increased rate of venous flow in 3. Because of the relief of the peripheral vascular spasm Apresoline is a suitable hypotensive agent for the treatment of toxaemia of pregnancy and biomicroscopy may help to determine the suitability of other hypotensive drugs.

Discussion

Mr. F. Stabler pointed out that vascular spasm was presumed to be widespread, but might not be so diffuse. It was this spasm that was presumed to account for the small babies. The uneven distribution of the spasm might account for the varying clinical pictures, and perhaps also these drugs were not of much value.

Mr. L. Snaith thought the effect of hypotensive drugs was not conclusive, though there was a possibility that the dosage was not big enough.

Mr. G. T. Johnson was of the opinion that the drugs were of value, but treatment had to be essentially symptomatic.

Mr. P. Malpas commented on the fall in blood pressure when the foetus died.

Mr. Tacchi, in reply, said that his work had been carried out because of the disappointment in the use of hypotensive drugs.

Professor J. K. Russell described

Combined Visual and Sound Teaching Aids in Obstetrics and Gynaecology

The use of a tape recorder was discussed in case-taking especially in such conditions as placenta praevia and ectopic pregnancy, and to illustrate operative technique. The case history of a woman with carcinoma of the cervix was run over, and a film was shown of the Wertheim's hysterectomy on this patient.

Discussion

Mr. L. Snaith asked if Professor Russell advocated disc recordings without the students.

Mr. S. Way was cautious, he emphasized that the visual aid we needed was the patient herself.

The President asked whether this method of teaching was for the purpose of illustrating how to take a history or was it intended as instruction on carcinoma of the cervix, because the real difficulty was the awkward patient.

EAST ANGLIAN OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

May 1960

A meeting of this Society was held at the Peterborough Memorial Hospital, on Saturday, 28th May, 1960, under the Chairmanship of the President, Mr. Michael Bulman.

Outbreak of a Haemolytic Streptococcal Infection in a Maternity Unit

Dr. B. W. Powell, the paediatrician, gave an account of his recent experience of such an outbreak in the nursery of the Thorpe Hall Maternity Unit. Thorpe Hall is an old mansion that has been converted into a maternity unit, and the babies are nursed in a common nursery. During February, 1960, a number of the infants had suffered from a pustular dermatitis and therefore a complete bacteriological survey of the staff and patients

had been carried out. No haemolytic streptococci had been detected although the haemolytic streptococcus type XII, the nephritogenic type, was known to be prevalent in the area. On 10th March, 1960, an infant, whose supernumerary toe had been treated by ligation, was found to have a marked inflammatory reaction around the toe due to the presence of a haemolytic streptococcus type XII. On 21st March, 1960, an infant died at home from an acute haemolytic streptococcal meningitis type XII two days after leaving the nursery and the following day a second baby died from the same illness. These disasters prompted a re-investigation of the maternity unit. Forty-six babies were at risk and 22 were found to carry a haemolytic streptococcus type XII on the umbilical stump. Eleven of the 22 became ill; 7 developed meningitis and 5 of these infants died; 4 had minor local infections. No mothers were found to be infected and only one member of the staff, who joined after the epidemic was under way, developed a streptococcal throat.

Hitherto the umbilical stumps had not been covered, but now they were covered with sterile dressings, after the application of a penicillin sulphonamide powder. It was hoped that this measure would stem the outbreak as the streptococcus was penicillin-sensitive, but it proved a failure, and only closure of the unit solved the problem. The original source of the infection remained undiscovered.

The wards and nurseries were fumigated, washed down, and repainted, but it was some time before the haemolytic streptococcus was eliminated.

Mr. Bulman thanked Dr. Powell for his interesting and very disturbing report. In the maternity unit in Norwich they had had two cases of *Clostridium welchii* infection, one of the patients died. A bacteriological investigation revealed the presence of the same organism in the dust on brooms, oxygen cylinder heads, and on shelves.

Other members took part in the discussion and pressed the advantages of the rooming-in technique and the use of an antiseptic on the umbilical stump.

Gynaecological Retrospect

Mr. J. C. Spry-Leverton addressed the Society on the development of our speciality and because of the limited time available restricted his review to the study of the lives of two prominent Victorians: James Matthew Duncan, a great obstetrician and the founder of the British School of conservative midwifery, and Robert Lawson Tait who, by his insight, courage and pugnacity, founded modern gynaecological surgery.

A Review of Cases of Uterine Sarcoma

Mr. Norman Kimbell reported 9 cases of uterine sarcoma that he had treated in the past eleven years. After a review of the macroscopic and microscopic characteristics of uterine sarcoma, he then gave a detailed account of his cases. Their ages ranged from 37 years to 76 years. The standard treatment was a total hysterectomy and a bilateral salpingo-oöphorectomy followed by a course of deep X-ray therapy. In one instance deep X-ray therapy had been successful in controlling a recurrence 2 years after the primary operation, but on two occasions X-ray therapy was not used; one mentally ill patient refused the treatment and, nevertheless, survived 8 years and a second patient was too ill for treatment. The results of his treatment have been encouraging. One patient has survived 10 years, 2 are alive 9 years after operation, one is well 8 years later, and there are survivals after 4 years and 3 years. One case has only just had her treatment. Two have died.

In the subsequent discussion it was apparent that only the radiotherapist at Peterborough had any faith in the value of deep X-ray in the treatment of uterine myosarcoma.

Mr. David Brown requested the views of the members on the treatment of a problem case. "A young woman medical student had a myomectomy performed and a sarcoma was detected in the centre of the tumour. Nothing further was done and she is alive 2 years later." The meeting endorsed the line of treatment adopted for this particular case.

BOOK REVIEWS

"Ovum Humanum." By LANDRUM B. SHETTLES, M.D., Ph.D. Pp. viii+79, 64 illustrations. Hafner Publishing Company, Inc., New York, 1960. Price 55*s*.

INTEREST in the development of the mammalian embryology dates from the dawn of medical science, and there was much speculation as to the origin of embryos. It was not, however, until 1827 that Von Baer discovered the mammalian ovum. The reviewer considers it unfortunate that Harvey, who was interested in embryology, used the roe deer (which exhibits delayed implantation) as his experimental animal for research in reproduction; if he had used one of the more common domestic mammals such as the dog or rabbit there is the probability that he might have found the ovum. Once the mammalia ovum had been recognized the science of mammalian embryology was established on a sound basis. It is a fact that between 1656–1672 Van Horne, Swammerdam, Stensen and de Graaf independently reached the conclusion that the mammalian ovaries —"female testes"—produced ova. Unfortunately de Graaf assumed the entire contents of the ovarian (Graafian) follicle to be the ovum. In 1930, Allen, Pratt, Newell and Bland recovered the first human ovum from the uterine tube.

The author of the present atlas is to be congratulated for giving us a pictorial presentation in sixty-four superb photomicrographs of the development, growth, maturation, ovulation, fertilization and cleavage of the human ovum.

In the caption of different illustrations the following topics, amongst many, are discussed and illustrated: the enzymatic action of the tubal mucosa on the corona radiata cells, the movements of the vitellus within the zona pellucida, the presence of two primary oöcytes within a single follicle and its possible bearing in twinning, and the nourishment of the ovum by the cells of the corona radiata. There is only one minor point of criticism; it is unfortunate that the magnifications were not included in each legend.

There is a short appendix which gives details of the methods used to obtain and photograph the eggs.

The book makes a valuable contribution to our knowledge of the development of the human ovum, and it can be recommended without reserve.

W. J. Hamilton

"The Clinical Value of Methyl Oestrenolone and of Allyl-Oestrenolone in Menstrual Disorders and in Pregnancy" (De Klinische waarde van methyl-oestrenolon en allyl-oestrenolon bij menstruatie stoornissen en bedriegde swangerschap). By H. WILLEMSEN. Pp. 88, with 12 photomicrographs. Rijksuniversiteit, Groningen, 1960.

THIS is an M.D. thesis presented at the University of Groningen in Holland this year. It is one of the first reviews to appear concerning the clinical application of the new progestational compounds which are profoundly affecting endocrine therapy in this field. It should have formed a useful addition to the American compendium of papers published in the Annals of the New York Academy of Science as the hand of drug companies is writ large in the latter. Unfortunately it is neither comprehensive nor critical. At least a compilation of the rapidly growing literature on this subject would be of value but Dr. Willemsen's bibliography is short, haphazard and appears to have altogether missed a number of definitive papers. In one respect he has pulled off a considerable coup; not a single British publication is cited. Naturally it is not possible to discuss pregnanediol without mentioning Marrian, but this reference, like a number of others, is not included in the bibliography.

The compound 17 methyl-17β-hydroxy-19-norandrost-4-ene-3-one (methandrolone), is produced by the Organon company and therefore of particular interest in Holland. It has not had a very enthusiastic reception elsewhere, because of reputed androgenicity. Dr. Willemsen used it in the treatment of amenorrhoea, of menorrhagia, of dysmenorrhoea and of threatened and habitual abortion. It appears that in the treatment of menstrual disorders methandrolone achieves results much the same as norethindrone and norethandrolone which are more commonly used in this country. In view of the fact that three mothers showed signs of masculinization and two developed jaundice, it is not surprising that Dr. Willemsen does not recommend the use of methandrolone in pregnancy.

A final section deals with the use of allyl-oestrenolone in the conservation of pregnancy. There have been almost no publications on the clinical use of this compound and it is a pity that the 30 patients treated by Dr. Willemsen do not constitute a sufficiently large or homogeneous group to give a reliable result. A properly designed therapeutic trial of this compound is desirable.

Arnold Klopper

"A Short History of Obstetrics and Gynecology." By THEODORE CIANFRANI, M.D. Pp. xvi+449, with 225 figures. Blackwell Scientific Publications Ltd., London, 1960. (Charles C. Thomas, Springfield, Illinois.) Price £5.

THIS book is intended for medical students and practitioners with little knowledge of obstetrics and gynaecology. The development of the subject is traced from the prehistoric period up to the present day and is correlated with the evolution of medical science as a

whole. Unfortunately the account lacks balance; the relatively scanty information available about pre-18th century obstetrics and gynaecology is presented in greater detail than is the subsequent development of operative techniques and principles of treatment. In addition, while the achievements of individuals are described, as is stated on the dust cover, "with just enough of the human element to make fascinating reading", comparatively little space is devoted to linking the work of these individuals into a common pattern of progress. The last 50 years are described too briefly; blood transfusion and the chemotherapeutic and antibiotic agents receive only one paragraph each, while the marked effect that the increased safety of Caesarean section has had on the stillbirth and neonatal death rates is mentioned only in passing. There is no reference to the discovery and use of ergometrine.

There are many illustrations, most of which are well chosen. It is questionable, however, whether later artists' impressions of earlier medical scenes should appear in a history book. The line illustrations of "the aborigines in the throes of complicated labour" are also of doubtful value.

As might be expected of a book costing five pounds, the printing and binding are excellent.

"Shaw's Textbook of Operative Gynaecology." Second edition, revised. By JOHN HOWKINS. Pp. viii+484. Illustrated. Livingstone, Edinburgh and London, 1960. Price £5 5*s*.

THIS book was first published in 1954 shortly after Wilfred Shaw's death. The second edition is by Mr. John Howkins who has not allowed reverence to unduly weight his appraisal of the original text. For example, descriptions of the fascia lata sling, interposition, Spalding-Richardson, Alexander-Adams and Le Fort operations have been eliminated. Surgical anatomy is still the theme of the entire book. Fasciae, inter-fascial plane and ligaments are meticulously described in an early chapter and are emphasized in the description and illustration of every operation.

New chapters describe exfoliative cytology, colposcopy, culdoscopy, carcinoma *in situ*, genital tuberculosis and radiotherapy. New sections cover the non-slip mattress, fractional curettage, the staging of endometrial carcinoma, utero-tubal implantation, the isolated ileal conduit and the management of cardiac arrest. The previous account of Howkins's synchronous combined abdomino-vaginal hysterectomy is considerably elaborated and pelvic exenteration is now described in detail.

Sound schemes are provided for selecting the best operative procedure in each situation; alternatives are kept to a minimum and some are wisely omitted. Complete guidance is given for the performance of each operation and the management of complications. There is a masterly section on urinary fistulae and a full account of alimentary lesions likely to be encountered in gynaecological practice.

The illustrations are unusually generous and their clarity and artistry are unique. The text is concise and well ordered, the print is large and the layout spacious. It is a most attractive book and easy to read. Adequate bibliographies, previously scant or absent, now follow approximately half of the chapters.

Possible improvements are few but it could have been pointed out that oral feeding has replaced the original Bull regime in the treatment of oliguria. Many would consider the course of treatment recommended for genital tuberculosis to be of insufficient duration. One of two techniques for vaginal hysterectomy in the presence of prolapse is rather unorthodox and the very small but definite place of classical Caesarean section could be more specifically defined.

This book now presents a selected and integrated summation of the views and practices of two master gynaecologists. It is of such outstanding merit that postgraduate students and registrars should make it their bible of operative gynaecology and many of their seniors could study it with advantage.

"A Textbook of Gynaecology." By PROFESSOR LAMAN A. GRAY (Louisville, Kentucky). Pp. xv+470, 324 figures+6 colour plates. Charles C. Thomas, Springfield, Illinois, U.S.A., and Blackwell Scientific Publications Ltd., Oxford. Price £6 4*s*.

THIS inspiring new textbook for the general practitioner and internist is by an Associate Professor of Gynaecology at Louisville who was a pupil of the late Thomas S. Cullen.

The book starts, not with forbidding recapitulation of anatomy, but with a wise chapter on doctor-patient relationship, followed by a useful one on gynaecological endocrinology. Subsequent chapters deal with the usual divisions of the subject and include full pathological and histological details. Operative technique is limited to illustrations of most standard procedures, though the author cannot resist some excellent plates of re-implantation of a stenosed ureter. The illustrations of abdominal hysterectomy show well the Richardson sub-fascial technique. The method of marsupialization of Bartholin's cysts is described and the author reminds us that not all cysts and abscesses of Bartholin's gland and Skene's ducts are Neisserian in origin. The chapter on gynaecological infections is excellent and elsewhere the less well known venereal diseases usefully described.

In line with current theory is the use of the term "eversion" of the cervix for erosion and the very high incidence in nulliparae is emphasized.

Epithelial changes leading to carcinoma of the cervix are well described as are the modern methods of diagnosis. Cytotoxic drugs receive adequate mention in the chapter on Ovarian Tumours. Hormone treatment of endometriosis by the Kistner pseudo-pregnancy regime is described in a good account of this condition which illustrates well the principles of conservative surgery.

The only marked deficit in the contents lies in a very brief treatment of abortion, without mention of internal os deficiency in late abortion and without discussion of habitual abortion. Taken with a long detailed chapter on

uterine abnormalities this suggests imbalance of presentation which is again noted by comparing the short section on the all too frequent complaint of menorrhagia, met daily by the practitioner, with the full chapter on endometriosis.

The text concludes with a useful contribution on psychosomatic gynaecology or "Gynaechiatry" by Dr. William K. Keller. This new term is of dubious acceptability.

The text is easy to read and the author has written an up-to-date contribution from his wide experience which should be useful to postgraduates as well as undergraduates. The illustrations are excellent if at times over large and the book is beautifully produced, without errors. The price is regrettably high, putting it outside the range of most undergraduates, and one feels that the colour plates could have been sacrificed as an economy.

SECOND INTERNATIONAL SYMPOSIUM ON STERILITY

VARENNA, LAKE OF COMO

18TH–20TH MAY, 1961

THE second Italian Symposium on Sterility will be held at the Villa Monastero, Varenna, Lake of Como, 18th to 20th May, 1961. All interested persons are invited to attend. The working languages will be Italian and English, with simultaneous translation.

Further details of the Symposium may be obtained from the Secretary: Dr. A. Chiara, Ospedale Provinciale di Maternità, Via Paoli, 28, Como, Italy.

REVIEW OF CURRENT LITERATURE

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OBSTETRICS AND GYNAECOLOGY

313. **The Proceedings of the Second Academic Conference of German-speaking Professors and Lecturers in Obstetrics and Gynaecology.** (Vorträge und wissenschaftliche Beiträge der 2. akademischen Tagung deutschsprechender Professoren und Dozenten für Geburtshilfe und Gynäkologie.)

Geburtsh. u. Frauenheilk., **20**, 505–808, June 1960.

Finland acted as the hosts for the Second Conference of German-speaking Gynaecologists, which was held in Helsinki from 30th July to 1st August, 1959; the June number of *Geburtshilfe und Frauenheilkunde* is entirely devoted to a complete report of the proceedings. The first of these conferences was held in Basel two years previously (reported in *J. Obstet. Gynaec. Brit. Emp.*, 1958, **65**, 671). The convener then was Professor Koller of Basel. His aspiration in calling such a conference was that workers of different nationalities, but using a common language, should exchange and discuss the results of research for the mutual benefit of their patients. Since the first conference a "Bureau for Obstetrics and Gynaecology" has been established, which has served as a means of exchanging and co-ordinating information and the results of research between German-speaking gynaecologists.

The Second Conference was attended by 75 delegates, who represented Austria, Denmark, Finland, Germany, Greece, Holland and Switzerland. There were 75 contributions (including films, exhibits and papers) which dealt with a wide variety of subjects. It is only possible here to mention some of the papers which were presented. Of considerable interest are the tables and graphs concerning the statistics of the maternity services, etc., in Finland. A striking finding was the correlation found in Finland between birth weight, placental size and maternal cardiac volume; a mother with a small heart under increased pressure of work was more likely to go into premature labour. Langreder compared various methods of external and internal tocography and concluded that the most valuable information could be derived by continuous recording of the circumference of the abdomen during labour. Andreas and Schmidt found that particles with a molecular weight up to 30,000 were capable of passing through the foetal membranes; the rate of diffusion was accelerated in the presence of electrolytes; diffusion was slower in the direction amnion to chorion. Oehlert found that on an average about 7 per cent of the haemoglobin in retro-placental blood was foetal in origin; in 29 of the 100 cases studied this figure rose to 59·9 per cent. Alex reported on finding the causative organisms of Listeriosis in smears of meconium taken from affected infants.

Kremling used the length of the urethra, measured from bladder neck to the ischial tuberosity on a lateral urethro-cystogram, as a diagnostic and prognostic criterion for the evaluation of stress incontinence. Schaetzing described his modification of Le Fort's operation, in which he obliterated the vagina by uniting the lateral walls, instead of the anterior and posterior walls. The photographs of Zinser's beautiful stereomicroscopic studies of the injected blood vessels of the human cervix are reproduced. Napp found that the administration of ethinyl nor-testosterone between the 12th and 14th weeks of pregnancy resulted in a temporary fall in oestrogen and pregnanediol excretion.

Peter J. Huntingford

PREGNANCY

314. **Plasma Adrenaline and Noradrenaline Levels during Pregnancy, Labour and in Pre-Eclampsia.** (Adrenalin- und Noradrenalin-Bestimmungen im Blutplasma in der Schwangerschaft, unter der Geburt und bei Schwangerschaftstoxikose.)

By E. HOCHULI. *Geburtsh. u. Frauenheilk.*, **20**, 835–842, July 1960. 25 refs.

Blood samples were obtained from normal men and women, from women during pregnancy, labour and the puerperium, and from those with severe pre-eclampsia. The concentrations of adrenaline and noradrenaline were estimated by means of the fluorometric method of Weil-Malherbe and Bone. The average normal values were as follows: women, adrenaline 0·873 ng per ml. (ng=10^{-9}G.) of plasma, and noradrenaline 2·185 ng per ml. of plasma; men, adrenaline 0·963 ng per ml. of plasma and noradrenaline 3·46 ng per ml. of plasma. This difference between men and women was significant, but was thought to be related to the amount of physical activity, which had preceded the withdrawal of blood. During prolonged and painful labour slightly raised, but not statistically significant, levels of adrenaline were found. No other significant alteration from the normal values was detected.

Peter J. Huntingford

315. **The Use of 6-α-Methyl-17-α-hydroxy-progesterone Acetate as a Test Substance for the Early Diagnosis of Pregnancy.** (Il 6-alfa-metil-17-alfa-idrossiprogesterone acetato quale sostanza test per la diagnosi precoce di gravidanza.)

By U. BOLOGNA and A. SALVATI. *Ann. Ostet. Ginec.*, **82**, 606, May 1960. 3 refs.

The synthetic progestogen 6-α-methyl-17-α-hydroxy-progesterone has been used as a diagnostic test for early pregnancy. This has been compared with the Galli-Manini test in 48 cases of women with 40 to 60 days amenorrhoea. The dose consisted of 40 mg. daily for three days. The test proved accurate in 98 per cent of cases, there being one false positive. The Galli-Manini tests on the same women gave two false negatives.

In cases of functional amenorrhoea, bleeding occurred 3 days after the drug was discontinued.

Josephine Barnes

316. **Genital Listeriosis as a Cause of Repeated Abortion.**

By F. RAPPAPORT, M. RABINOVITZ, R. TOAFF and N. KROCHIK. *Lancet*, **1**, 1273–1275, June 11, 1960. 2 tables. 10 refs.

Thirty-four patients attending the Hadassah Municipal Hospital in Tel Aviv, Israel, with a history of repeated abortions were investigated for the presence in the genital tract of micro-organisms belonging to the genus listeria. Samples of cervical secretion were cultured and listeria organisms were grown in 25 of the 34 patients. By contrast there were no positive cultures in 87 control patients who had no history of abortions. The affected patients were treated with a 14-day course of penicillin (1 million units daily) and sulphamethoxypyridazine (1 g. daily). It was found that the cervical cultures became negative during the treatment but that re-infection occurred 1 to 6 weeks later. A long-term maintenance dose of sulphamethoxypyridazine (0·5 g. daily) appears to be advisable. In 8 of the 25 positive cases the diagnosis was made in the first trimester of pregnancy. None of these patients aborted after treatment.

The authors point out that listeriosis is an accepted cause of abortion in domestic and wild animals; they are of the opinion that a similar relationship exists in women when a continuous excretion of listeria organisms from the cervix can be demonstrated over a long period.

J. M. Brudenell

317. **The Value of Progesterone Treatment of Threatened Abortion.** (Valeur du traitement par la progesterone au cours de menaces d'avortements.)

By H. DE WATTEVILLE. *Ann. Ostet. Ginec.*, **82**, 848, May 1960.

Progesterone has long been used for the treatment of threatened abortion but the effects have been disappointing, and in the author's experience superior results have been obtained so far by the use of stilboestrol. The explanation of this may lie in the fact that abortion is not often provoked by deficiency of progesterone or that the doses administered were inadequate to substitute for deficient secretion.

Pregnanediol excretion is lowest in these cases of spontaneous threatened abortion where treatment proves unsuccessful. The lowest levels are in those of missed abortion or "blighted ovum" where there is no embryo.

The importance of incompetence of the cervical os as a cause of abortion is now well known. One must also not neglect inflammation of the membranes or placenta as another possible cause.

Recently low oestrogen levels have been found in women with threatened abortion and this factor must always be borne in mind.

Treatment with very large doses of progesterone intramuscularly, up to 4 grammes a day, has been recommended. This is not well tolerated by the tissues.

Progesterone is no panacea for the treatment of threatened abortion but in cases where pregnanediol excretion is low, adequate substitution therapy should be given. The new synthetic progestogens permit a more complete substitution and this should bring about a greater percentage of success than formerly.

Josephine Barnes

318. **Premature Separation of the Placenta.**

By D. TORUP and J. WIELANDT. *Acta obstet. gynec. scand.*, **39**, 291–315, 1960. 17 figs. 23 refs.

This is a study of 211 cases of premature separation of the placenta which occurred at the Maternity B. Department of Rigshospitalet Copenhagen, in the decade 1946–55.

The incidence of the condition was 1 per cent; parity was of no significance in the incidence or severity of

the separation. Only one case was of traumatic origin. Toxaemia was present in 31·2 per cent of cases. The maternal mortality was nil, but the perinatal foetal loss was 48·5 per cent; 60 per cent of the infants were premature; the perinatal foetal loss of infants weighing over 2,500 g. was 37 per cent. Afibrinogenaemia occurred 4 times.

The treatment was conservative and consisted of morphine, blood-transfusion, rupture of the membranes, oxytocics, forceps delivery (10·4 per cent of all cases), and perforation of the presenting foetal head in 4 cases of intra-uterine death. Caesarean section was done only twice in the whole series.

The authors recommend conservative treatment on these lines if the foetus is expected to weigh less than 2,500 g., but they propose to do a Caesarean section if the foetus is alive and estimated to weigh over 2,500 g., if the maternal condition is good, and if there is no other possibility of rapid delivery. The authors expect to reduce the infant loss in the group exceeding 2,500 g. from 37 to 25 per cent, and in the entire series from 48·5 per cent to 43 per cent.

[The authors have been fortunate not to encounter the complication of obstetric anuria.] *N. Alders*

319. **Biology of Severe Vomiting at the Onset of Pregnancy.** (Considérations sur la biologie des vomissements graves du début de la grossesse.)

By M. Rivière, L. Chastrusse, J.-P. Dubecq and G. Maleviale. *Gynéc. et Obstét.*, **59**, 18–46, Jan.–Mar. 1960. 8 tables. 14 graphs. 66 refs.

This is a record of observations carried out on 30 patients with severe enough vomiting to require replacement therapy, usually intravenously, during the first three months of pregnancy.

Sixteen patients were primigravid and 14 multiparous. Of these 5 had already shown signs of severe vomiting in previous pregnancies. The age range was 19 to 35.

The paper is valuable because it sets out the normal levels of blood electrolytes in the non-pregnant woman and the normal quantities of urinary electrolytes eliminated in 24 hours.

Tables indicate the opinions of various authors as to what the electrolyte levels should be during pregnancy as compared with the non-pregnant state; and the normal elimination of cortico-steroid hormones in the non-pregnant and the pregnant state.

Graphs show the various readings for the various electrolytes that the authors obtained in control patients and in their own series of ill patients. Fifty-five of the references cover a great deal of what is known and has been written about the subject since 1950; only 11 are from before that date.

The authors' conclusion is that starvation is the main result of severe vomiting, and that the dangers arise more from the results of the starvation than from the actual losses caused by the vomiting.

[The paper should be very valuable as a reference paper for people interested in this particular subject.]

Elliot E. Philipp

320. **Aldosterone and Pregnanediol Excretion during Normal and Toxaemic Pregnancies.** (Aldosteron- und Pregnandiol-Ausscheidung im Urin der normalen Schwangerschaft und der Toxikose.)

By N. C. Louros, K. Miras and L. Frangiadakis. *Geburtsh. u. Frauenheilk.*, **20**, 848–851, July 1960. 19 refs.

Aldosterone and pregnanediol excretion were measured in 13 normal pregnant women, in 5 with oedema and in 5 with pre-eclampsia. The aldosterone output varied between 24–88 μg. per 24 hours, during normal pregnancy; in those with oedema or toxaemia the range was 26–65 μg. per 24 hours. Neither was there any difference in the pregnanediol excretion of these patients; the range of values obtained was 22–59 mg. per 24 hours.

Peter J. Huntingford

321. **Effect of Extracts of Blood and Placenta from Normal and Toxic Patients on Oxidative Phosphorylation.**

By C. R. Hoover and R. A. Bartholomew. *Obstet. and Gynec.*, **16**, 57–61, July 1960. 2 tables. 4 refs.

The concept of the placental origin of toxaemia of pregnancy implies that placental infarction and anoxia may result in the liberation into the maternal blood of a toxic substance. The authors have tested the hypothesis that this substance might be capable of uncoupling oxidation from phosphorylation, since oxidative phosphorylation systems are notorious for their sensitivity to low concentrations of several substances.

In the complex and rather delicate tests, no difference was found in the effect of placental and plasma extracts from normal and toxaemic patients on the ability of rat liver mitochondria to undergo oxidative phosphorylation.

J. G. Dumoulin

322. **A Contribution to the Subject of Phaeochromocytoma in Pregnancy.** (Ein Beitrag zum Phäochromozytom in der Schwangerschaft.)

By M. Erfurth. *Zbl. Gynäk.*, **82**, 939–944, June 18, 1960. 1 illus. 18 refs.

With the increasing knowledge of causes of hypertension the proportion of cases labelled as "essential" is diminishing. A rare but important cause is phaeochromocytoma (PH).

The author reports one such case in detail in a woman of 35 years with circulatory crises. When the pregnancy had reached 38 weeks intra-uterine death occurred. The patient had albuminuria and a blood pressure of 225/140 and was thought to be suffering from pre-eclamptic toxaemia. A macerated foetus was born a few days later. During the subsequent few days the blood pressure varied between 220/130 and 130/85. On the seventh day of the puerperium the patient had a secondary haemorrhage and the uterus was explored. Ten hours later she developed the clinical picture of shock and died in a condition of circulatory collapse. At post-mortem examination a phaeochromocytoma was discovered in the left suprarenal gland.

The author discusses the diagnostic problem of PH and suggests the following investigations; (1) On palpation of the affected kidney adrenaline is poured out and may cause a paroxysm of hypertension. (2) Adrenolytic or sympatheticolytic substances should lower the blood pressure by at least 35 mm. Hg. (3) The histamine test. (4) Demonstration of pressure amines in the urine.

Bruce Eton

323. **Foetal Mortality in Essential Hypertension.**
By J. M. GATE. *Lancet*, **1**, 901–902, April 23, 1960. 7 refs.

The author has analyzed the foetal outcome in a series of 71 patients in whom the blood pressure was 150/100 or over before the 20th week of pregnancy. There were 4 stillbirths and 1 neonatal death, a total foetal loss in the whole series of 8 per cent. Thirty patients (42 per cent) developed superimposed pre-eclampsia and 4 of the foetal losses occurred in this group. The patients were treated by long periods of rest coupled with sedative drugs. In a few cases antihypertensive drugs were used. No patient was allowed to go beyond full term. Surgical induction was performed in 26 (37 per cent) cases. The Caesarean section rate was 21 per cent.

The author concludes that with modern obstetric care a better foetal prognosis can be given than formerly in these hypertensive patients.

J. M. Brudenell

324. **Infective Jaundice in Pregnancy.** (Epatite itterigena infettiva in gravidanza.)
By E. FERRARIO. *Minerva ginec.* (*Torino*), **12**, 592–607, June 30, 1960. 11 graphs. 7 tables. 108 figs.

Eleven cases of jaundice in pregnancy are detailed. The jaundice appeared at all stages of pregnancy from the 23rd week up to full-term. In their main features, all the cases appeared to be indistinguishable from the epidemic virus type of jaundice. In other words, these were cases of jaundice associated with pregnancy and not *due* to it. All the mothers recovered after varying lengths of illness and went into labour whilst jaundiced or after recovery. Treatment was on general lines.

Where the jaundice appeared early in pregnancy, the child born at or near term was unaffected. Where labour was induced on account of the severity of the symptoms (at 34 and 32 weeks) the child did not survive. Foetal mortality was 2 intra-uterine deaths and one in the neonatal period. The virus is presumed capable of passing the placental barrier.

Preceding the jaundice, the usual symptoms were anorexia, nausea, weakness and malaise. Enlargement of the spleen was much more often observed than that of the liver. Whilst not denying the occurrence of a true acute atrophic jaundice in pregnancy with its very high mortality rate, the author considers the early differentiation (apart from the feature of concurrent local epidemic jaundice) difficult, although yellow atrophy of the liver is usually associated with other signs of toxaemia of pregnancy.

W. C. Spackman

325. **Effect of Chlorothiazide on Insulin Requirements of Pregnant Diabetic Women.**
By M. LAKIN, I. ZEYTINOGLU, M. D. YOUNGER and P. WHITE. *J. Amer. med. Ass.*, **173**, 353–354. May 28, 1960. 3 refs.

Chlorothiazide is now used at the Joslin Clinic in the treatment of pregnant diabetics to prevent the formation of polyhydramnios. It has now been given throughout pregnancy to 61 cases and these were investigated by the authors to determine whether chlorothiazide, being a sulphonamide, affected insulin requirements. Compared with a control group the chlorothiazide treated patients exhibited a 10 per cent weight reduction, but no difference was found in insulin requirements either during or after pregnancy. The serum potassium level was not affected by the use of chlorothiazide in the pregnant diabetic. This was thought to be due to the fact that the diet of a pregnant diabetic is high in potassium and so potassium supplements were not given.

D. W. James

326. **A Contribution to the Diagnosis of Extra-uterine Pregnancy.** (Ein Beitrag zu Diagnostik der Extrauterin-gravidität.)
By H.-J. STAEMMLER. *Zbl. Gynäk.*, **82**, 857–863, June 4, 1960. 3 tables. 48 refs.

The diagnosis of extra-uterine pregnancy is based on the history, general and pelvic physical signs, biological pregnancy tests, aspiration of the pouch of Douglas and curettage. The author reports his observation on the basal temperature in four cases of ectopic pregnancy in which records had been kept. The initial Hogben test was negative in all. Curettings were not diagnostic in three; the fourth patient was not curetted. Aspiration of the pouch of Douglas performed in two patients yielded blood in one but not in the other. The basal temperature however showed the rise characteristic of pregnancy in all four patients.

The author concludes that in cases of suspected ectopic pregnancy observation of the basal temperature should be regarded as a diagnostic aid.

Bruce Eton

LABOUR

327. **The Grand Multipara: Some Italian Figures.** (Considerazioni sulla gravidanza. Il parto e il puerperio nell grandi multipare.)
By L. SBROCCA. *Minerva ginec.* (*Torino*), **12**, 511–512, May 31, 1960. 9 refs.

In contrast to some American statistics, a small series for 80 Italian women is presented. They relate to women who have had from 7 to 13 children. Whereas the American figures show the incidence of abnormal presentation, twins, post-partum haemorrhage and hypertensive nephropathy as double, and for accidental haemorrhage and prolapse of the cord as treble that applicable to lower parities, the Italian figures showed completely normal deliveries in 79 of the 80. Foetal loss for the 81 babies born was two, one due to cord prolapse

and one to gross foetal abnormality. The presentation was cephalic in 75, breech in 5 and one as face. The author concludes that, as regards Italian women at any rate, the risks of grand multiparity may not be as great as is sometimes supposed. *W. C. Spackman*

328. **Posture in Obstetrics.**

By K. B. Rao. *J. Obstet. Gynaec. India*, **10**, 486–490, June 1960. 21 refs.

It may be of interest to obstetric historians that the dorsal position was used for delivery in India, in the Rig Vedic days about 1500 B.C. This position remained in favour in ancient India, according to Buddhist texts, although at the nativity of Buddha himself, the child is depicted as being born with the mother standing erect, supported by her sister and a Sal tree. In ancient China too, the dorsal position was used, bamboo rods being suspended from the ceiling to give support in the second stage.

In ancient Egypt, the woman retired to a corner with two female relatives, and the statues of two deities, and sat on her heels on some flat stones to allow space beneath for delivery of the child. Later, stones were replaced by stools as is mentioned in Pharaoh's edict "When ye do the office of a midwife to the Hebrew women, and see them upon stools, if it be a son, then ye shall kill him; but if it be a daughter, then she shall live".

The custom of delivery on a stool apparently spread eastwards to China, and westwards to Europe where they were employed during the Renaissance. The refinement of cushions came later, to avoid foetal injury. In Syria rocking chairs were used.

In sixteenth century England, stools were apparently still popular, but they fell into disuse in the seventeenth century, when the left lateral position was seemingly adopted, and was recommended in the Rotunda hospital in the eighteenth century. In rural Ireland and Cornwall in the nineteenth century, the kneeling position was used and version was done, and forceps were applied in this position. Walchers' position (which it seems had already been used by Albuccasis in the tenth century), had a brief popularity, followed by the exaggerated lithotomy position in the early twentieth century.

In India today, the dorsal position is once more in vogue, the obstetric stools being used only by the obstetricians. *John McKiddie*

329. **Blood Progesterone Levels in Relation to Parturition.**

By R. V. Short. *J. Reprod. and Fertil.*, **1**, 61–70, 1960. 1 table, 1 fig. 57 refs.

After a discussion of the theories of hormonal mechanisms which may initiate parturition in the human female and in animals, the author describes the results obtained by the use of a sensitive and specific method for the chemical determination of progesterone in the peripheral blood.

It was found that, in the case of the human female, the blood progesterone level rose steadily from the 11th to the 36th week of pregnancy and that a more rapid rise then followed, the level remaining high even during the second stage of labour, suggesting that the placenta remains an efficient endocrine organ at the time of parturition. It is pointed out that the late rising blood levels may result from a decreased rate of progesterone metabolism rather than an increased rate of production.

After discussing results obtained in animals, the author concludes that, in the human female, there is no evidence to suggest that progesterone is involved in the mechanism of parturition. *A. E. R. Buckle*

330. **Progesterone and 6-Methyl-17-hydroxyprogesterone Acetate in the Treatment of Threatened Premature Labour.** (Il progesterone ed il 6-Metil-17-idrossi progesterone acetato nel trattamento della minaccia di parto prematuro.)

By U. Ciulla. *Ann. Ostet. Ginec.*, **82**, 537, May 1960. 2 figs. 28 refs.

The author has compared the effects of injection of large doses of progesterone and oral administration of the new synthetic progestogen 6-methyl-hydroxyprogesterone acetate in the prevention of premature labour. The effects have been studied by means of electric recordings of uterine activity and these records have been used to adjust the dose to the needs of individual cases.

Progesterone by injection and smaller doses of the synthetic progestogen by mouth have been shown to be effective in preventing the onset of premature labour.

Josephine Barnes

331. **A Test for Ruptured Membranes.** (Un nuovo metodo per accertare la rottura delle membrane negli ultimi mesi di gravidanza.)

By T. Bacay and T. Wierdis. *Minerva ginec.* (*Torino*), **12**, 271–273, Mar. 15, 1960. 5 figs. 14 refs.

There is sometimes doubt whether the amniotic sac is intact or leaking in the last weeks of a pregnancy. Various tests have been proposed to help clear up the point. Lanugo hairs or fragments of foetal skin in any liquid obtainable can be looked for, but such tests are subject to error and are neither easy nor reliable.

The test proposed by the authors, and stated by them to be both simple and trustworthy, is the well-known fern-leaf test on crystallization of cervical mucus during the proliferative phase of oestrogenic activity (which disappears as soon as the secretory phase becomes established under the influence of progesterone whether natural or therapeutically administered). They have found that fern-leaf crystallization occurs in any fluid from the vault of the vagina when the fluid contains liquor amnii, but the test is negative if the membranes are intact.

[An obvious advantage of this test would be its suitability for use in the antenatal clinic or in out-patient or domiciliary practice.] *W. C. Spackman*

332. **A Method of Abdominal Decompression in Labour.** By D. B. Scott and J. D. O. Loudon. *Lancet*, **1**, 1181–1183, May 28, 1960. 7 figs. 3 refs.

The authors have developed an apparatus for applying a negative pressure to the abdomen during the uterine contractions of the first stage of labour. The idea of drawing the abdominal wall forward by this means to enable the uterus to become spherical during a contraction instead of being deformed into an ovoid was first advocated by Heyns (*J. Obstet. Gynaec. Brit. Emp.*, 1959, **65**, 189). The apparatus described in the present paper differs somewhat from that of Heyns. It is claimed to be cheaper and has the advantage that the patients' legs are free. A detailed description of the apparatus is given; it consists essentially of a polythene bag connected to a suction apparatus. The patient is placed in the bag, an air space over the abdomen being maintained by a steel cage inside the bag.

The apparatus has been used on patients in the Simpson Maternity Pavilion at Edinburgh and although no exact data are yet available the authors are impressed with results obtained and substantiate Heyns' claims that the first stage of labour can be both speeded up and rendered largely painless by this means.

J. M. Brudenell

333. **Epidural Anesthesia in Obstetrics and Gynecology.** By S. Norris, L. J. Harris and S. M. Eisen. *Obstet. and Gynec.*, **16**, 15–20, July 1960. 14 refs.

This is a report on 9,000 obstetric cases in which epidural anaesthesia was used together with a smaller number of gynaecological cases. In the technique used, the patient was either sitting or lying on her side. A 16–17 gauge Tuohy needle, 4 inches long and having a curved, blunt point, is inserted into the epidural space, and 18 ml. of 2 per cent xylocaine injected into the second or third lumbar space. The patient is put immediately into the lithotomy position. Full anaesthesia is attained in 5–18 minutes, and the effect lasts about 90 minutes.

There is usually a slight fall in blood pressure, thought to be due to about 10 per cent of the anaesthetic travelling into the subarachnoid space along the sheath of the penetrating nerves. Only 2 complications were encountered: total spinal anaesthesia occurred 3 times without fatality. Convulsions occurred 3 times, but these were satisfactorily controlled. There was no case of infection and no maternal death due to anaesthesia in the series. No serious neurological complications were experienced. The perinatal mortality seemed to be lower than with other anaesthetic methods.

J. G. Dumoulin

INFANT

334. **A Method of Identification of the Newborn in Maternity Hospitals.** (La plantigrafia neonatale quale mezzo di identificazione.)

By C. Cappetti and G. Colla. *Minerva ginec.* (*Torino*), **12**, 583–590, June 30, 1960. 28 figs. 26 refs.

To avoid possible mixing-up of newborn babies the method of taking the infant's foot-print is advocated. This involves stamping the imprint of its foot, rapidly cleansed with soap and spirit, on a chart provided and immediately placing beside it the mother's finger print. On its discharge from hospital, the footprint is again recorded beside the original one. A pad of printer's ink is used and the procedure is carried out before the baby is placed in its cot immediately after birth.

W. C. Spackman

335. **Hyperbilirubinaemia in Premature Infants and the Effect of Synthetic Vitamin K.**

By B. Corner and E. Berry. *Lancet*, **1**, 715–717. Apr. 2, 1960. 1 table. 3 figs. 14 refs.

The authors have examined the occurrence of hyperbilirubinaemia and kernicterus in premature babies without evidence of haemolytic disease. Between 1948 and 1954 kernicterus unassociated with isoimmunization was found post-mortem in 67 (2·6 per cent) of 2,599 premature babies nursed in the 2 units at Bristol. In 1954 the incidence of kernicterus fell sharply coincidentally with a change in routine management of the premature babies whereby "Vikastab", menaphthone dipotassium sulphate, was substituted for "Synkavit" and "Kappiodone", tetrasodium 2-methylnaphthalene-1:4 diol phosphate. It was therefore decided to study the effect of "Vikastab" in different doses on the serum bilirubin level. All babies weighing 5 pounds 8 ounces or less who did not show any evidence of Rh, ABO or other blood group incompatibility were included in the study. The serum bilirubin was measured repeatedly during the first few days of life by a modified Evelyn and Malloy technique. In all, the results of 436 cases were available for the final assessment of results. These were divided into 4 approximately equal groups according to the vitamin K dosage. Group 1 received no vitamin K at all, Group 2 received 5 mg. of "Vikastab" during the first 2 days of life, Group 3 between 10 and 15 mg. and Group 4 between 30 and 60 mg. The cases in each group were further subdivided according to their gestational age.

The results obtained lead the authors to conclude that hyperbilirubinaemia is primarily related to immaturity. "Vikastab" given in divided doses up to a total of 60 mg. in the first 2 days of life does not influence the development of hyperbilirubinaemia and does not increase the risk of kernicterus.

[The close correlation between "Synkavit" dosage and the level of serum bilirubin has been demonstrated by several workers. Where it is considered desirable for a newborn infant to be given a water soluble vitamin K analogue it would seem that "Vikastab" is quite safe and can be given in considerably higher dosage than "Synkavit".]

J. M. Brudenell

336. **Neonatal Hyperbilirubinaemia.**

By A. E. Claireaux. *Brit. med. J.*, **1**, 1528–1534, May 21, 1960. 71 refs.

Probably 40 per cent of infants have a serum bilirubin level of at least 4 mg. per 100 ml. during the first week

of life. In certain circumstances the level may be high enough to cause kernicterus even in the absence of an actual disease process such as haemolytic disease of the newborn. There is a danger therefore that jaundice in otherwise normal infants may be regarded as physiological and that corrective treatment may be started too late. Excessive serum bilirubin levels are most likely to be found in premature infants and babies with impaired liver function. In these cases there is delay in converting the toxic bilirubin to harmless bilirubin glucuronide, with the result that serum bilirubin levels rise to possibly dangerous levels. A table is submitted which lists the conditions leading to jaundice in the newborn and their likely relationship with kernicterus. The conditions are discussed in some detail.

In 1956 Meyer found that in the infant under 2,000 g. birth weight the serum bilirubin was still rising on the sixth day of life, whereas in the mature infant the peak was past by this time. Kernicterus was noted when the bilirubin rose to over 18 mg. per 100 ml.

Crosse *et al.* (1958) found that 8·4 per cent of 1,320 premature infants required blood transfusion because of dangerously high bilirubin levels. No infants with a level below 20 mg. per 100 ml. developed kernicterus, but 19 per cent of those with levels of 22–27 mg. per 100 ml. and 33 per cent of those with levels over 30 mg. per 100 ml. did develop the condition. It seems probable, however, that only 1–2 per cent of premature babies develop hyperbilirubinaemia under normal conditions.

Kernicterus may follow therapeutic measures. Excessive administration of vitamin K analogue ("Synkavit") either to the mother in labour or subsequently to a premature infant can result in liver damage and consequent hyperbilirubinaemia. Treatment of premature babies with Gantrisin (sulphafurazole) may cause kernicterus even though serum bilirubin levels are under 15 mg. per 100 ml. In this case it seems that the substance competes with bilirubin for attachment to plasma albumin so that the amount of disassociated bilirubin in the blood rises. Salicylates apparently act in a similar way.

Kernicterus is not uncommon in mature babies in Singapore. This may be due to poor liver function following on maternal malnutrition or to some unknown specific factor.

R. W. Grayburn

337. **The Effect of Intragastric Oxygen on the Oxygenation of Arterial and Portal Blood in Hypoxic Animals.**

By R. V. Coxon. *Lancet*, **1**, 1315–1317, June 18, 1960. 3 figs. 14 refs.

Intragastric oxygen is commonly used in Great Britain in the treatment of neonatal asphyxia. Quantitative evidence of its efficacy has not been forthcoming, and it has been suggested that factors other than the actual passage of oxygen over the gastric mucosa are responsible for the improvement in oxygenation which it frequently produces.

The author has investigated the changes in oxyhaemoglobin content of the arterial and portal venous blood in the hypoxic experimental animal following the administration of intragastric oxygen. Twenty adult cats, 2 kittens and 2 puppies were used in the investigation. The animals were anaesthetized and then rendered hypoxic by collapsing one or both lungs. Oxygen was administered at a rate of 0·5–1·0 litre per minute through a plastic tube passed into the stomach. Blood samples were taken by means of cannulas passed into the femoral artery and the portal vein. The results obtained showed that no increase occurred in the oxyhaemoglobin content of either the arterial or the portal venous blood after intragastric oxygen.

The author points out that the conditions under which the experiments were carried out were very different from those encountered when administering intragastric oxygen in the management of asphyxia neonatorum; in the circumstances these results alone do not constitute a reason for abandoning this resuscitative method. They do, however, point to the need for more quantitative information on its value than is at present available.

J. M. Brudenell

338. **Leukocytic Infiltration of the Umbilical Cord.**

By R. Dominguez, A. J. Segal and J. A. O'Sullivan. *J. Amer. med. Ass.*, **173**, 346–349, May 28, 1960. 4 figs. 4 refs.

Leucocytic infiltration of the umbilical cord, which was previously attributed to syphilis, is now believed to be significant in relation to foetal distress. The authors report upon the examination of 986 umbilical cords from single births at Saint Luke's Hospital to correlate the presence or absence of leucocyte infiltration with a number of maternal and foetal factors associated with foetal distress and anoxia.

Infiltration, which was found in 24·8 per cent of cases, refers to the blood vessels of the cord, primarily the vein. Two segments were examined in each case, one from near the placenta and one from the severed end. A significant association was found between leucocytic infiltration and (*a*) meconium staining of the liquor, (*b*) positional abnormalities of the cord, and (*c*) prolonged labour. A suggestive association was also found in general anaesthesia, grand multiparity and alteration in foetal heart rates.

The role of infection is discussed but there is no convincing evidence of direct association of leucocytic infiltration and intra-uterine infection. The authors conclude that leucocytic infiltration of the cord is due to interference with the normal blood flow in the umbilical vessels, and that retrospectively it is a more sensitive indicator of foetal distress due to hypoxia than the usual clinical signs. This might be useful in a long-term study of children to determine the effect of intra-uterine hypoxia on their ultimate development.

D. W. James

339. **Advantages of Delayed Tying and "Milking" of the Umbilical Cord.** (La curva ponderale nella prima settimana di vita dei neonati sottopost i ad emotrasfusione placentare mediante spremitura del funicolo.)

By T. ARCHILEI and E. BRACCO. *Minerva ginec. (Torino)*, **12**, 323–327, Mar. 31, 1960. 5 tables. 5 graphs. 15 refs.

It is estimated that immediately after birth for every 100 ml. of blood in the foetus there remain 30 ml. in the placenta and cord, and that with the common practice of immediate clamping or tying of the cord most of this blood is lost. It is of course impossible to secure for the foetus all this wasted blood, but by delaying the tying of the cord until it ceases to pulsate and by milking it towards the baby (the so-called physiological haemotransfusion) a useful quantity is gained. This principle was even enunciated by Darwin in 1801. The method is one of the standard ways of resuscitating an asphyxiated baby by pushing the better-oxygenated placental blood to where it can rapidly reach the vital centres of the infant's brain. Moreover, especially in premature or feeble babies, the additional supply of nutritional substances, pre-formed and immediately available, hormones and vitamins, salts, haemoglobin and water, is of great value.

The process is facilitated by normal retraction of the uterus in compressing, detaching and separating the placenta, by the infant's own heart action drawing blood through the umbilical vein, and by gravity if the child is held at a substantially lower level than the mother till the process is regarded as complete.

The authors further tested the advantages by comparing the weight loss or gain in the first eight days of life of 100 babies treated by delayed tying and active milking of the cord, as compared with 100 otherwise comparable babies after immediate ligature. They found that on average babies of the latter group were well below their birth weights after eight days, whereas in the former group there was a modest gain over their birth weight; correspondingly, the early loss of weight was substantially more in the immediate-ligature group, as strikingly demonstrated by the graphs accompanying the article.

W. C. Spackman

340. **Perinatal Mortality.**

By T. KAERN. *Acta obstet. gynec. scand.*, **39**, 392–437. 1960. 3 figs. 69 refs.

This paper from the Department of Obstetrics, St. Joseph's Hospital, Copenhagen, represents one of the opening lectures given before the Eleventh Congress of the Scandinavian and Finnish Association of Obstetricians and Gynaecologists in Helsinki, in August, 1960.

Perinatal mortality is defined as the number of infants dying before birth, during labour, or in the course of the first 7 days after birth, and weighing more than 1,000 g. at birth.

The study is based on a 30 months' survey (1st January, 1957 to 30th June, 1959) during which there were 549 perinatal deaths out of a total of 24,313 infants born, an incidence of 2·26 per cent. One hundred and ninety-seven of the infants that were lost weighed more than 2,500 g., and 352 weighed between 1,001 and 2,500 g. Twenty-five per cent of all perinatal deaths occurred before commencement of labour, 28 per cent during labour, and 47 per cent after birth. Sixty-four per cent of all perinatal deaths occurred among the 9 per cent of premature births of the series.

The causes of perinatal death per 1,000 births were as follows: malformation, 2·2; erythroblastosis, 0·5; infection, 0·4; trauma, 1·7; hypoxia, 14·7; unknown causes, 3·1.

The author suggests the following criteria for priority hospital admission.

(*i*) All those in the demographic risk groups. By demographic factors are meant circumstances in which an association has been established more frequently with perinatal death than with birth in general, such as social factors, age, parity, previous perinatal death.

(*ii*) All those suffering from a disease which is known to give an increased risk, although not specific for pregnancy.

(*iii*) All those who show signs of specific disease of pregnancy, no matter the degree of severity.

(*iv*) All multiple pregnancies.

(*v*) Breech presentations recognized 4 weeks before term or at the commencement of labour. All transverse positions. All atypical vertex presentations recognized before termination of labour.

(*vi*) All premature births more than 3 to 4 weeks before term, either at the commencement of labour, or transfer of mother and infant immediately after birth.

(*vii*) During labour all the major abnormalities should be transferred to hospital, namely toxaemia, haemorrhage, hydramnios, prolapsed cord, anomalies of uterine contractions, premature rupture of membranes (if contractions have not started after 12 hours), primigravidae who have been in labour for 18 hours without progress, multigravidae who have made no progress for 12 hours.

(*viii*) All infants who are moderately to severely anoxic, or show signs of disease should come into hospital.

[This paper is distinguished by great clarity of presentation, and is well worth detailed study, even if some of the author's recommendations may be controversial.]

N. Alders

341. **The Perinatal Mortality in Cases of Diabetes.** (Die perinatale Mortalität bei Diabetes.)

By H. LANGE. *Zbl. Gynäk.*, **82**, 1025–1031, July 2, 1960. 2 tables. 33 refs.

The author discusses the well-known problem of the high perinatal mortality of the children of diabetic mothers. Thorough treatment and close supervision of maternal diabetes are factors which improve foetal survival. The author's statistical analysis of 251 patients who required insulin showed that a gross perinatal mortality of 12·9 per cent was achieved by (1) a comparatively high insulin dosage, aiming at nearly normoglycaemic levels and (2) delivery about 3 weeks before the expected date. Improved results were noted particularly as regards intra-partum and neonatal deaths. The commonest type of foetal death was respiratory, due to anoxia, aspiration of liquor and hyaline membrane.

Amongst the last 50 cases of the series the perinatal mortality was reduced to 6 per cent, i.e., 3 cases of which two were intra-uterine deaths. *Bruce Eton*

OBSTETRIC OPERATIONS

342. **Use of a Vacuum Extractor (Ventouse) in Obstetrics.**

By J. A. CHALMERS and R. J. FOTHERGILL. *Brit. med. J.*, **1**, 1684–1689, June 4, 1960. 38 refs.

The use of the vacuum extractor (Ventouse) in obstetrics is described, the literature surveyed, and the author's experience of 100 cases delivered by means of the Malmström instrument recorded.

In 88 cases delivery was successfully completed with the Ventouse alone. In 12 cases extraction was started with the Ventouse but completed with forceps. In 8 of these, however, conditions were improved by the Ventouse in that the cervix was dilated and/or rotation and descent of the head were obtained prior to the application of forceps. Full dilatation of the cervix had been achieved in 84 cases, but on 16 occasions the Ventouse was applied prior to full dilatation because of inertia, foetal distress or presence of a uterine scar. General anaesthesia was used in 10 cases, in 5 of which forceps were applied after failure with the Ventouse. The instrument was used successfully in 2 cases of brow presentation and 3 cases presenting as frank breeches.

All the infants, whose weights ranged from 4 pounds 8 ounces to 11 pounds 2 ounces, were born alive except for 2 cases in which intra-uterine death of the foetus had previously occurred. There were 2 neonatal deaths. One followed final delivery by forceps for foetal distress, and the second was a first twin weighing 4 pounds 8 ounces which died from tentorial tears 6 hours after an early delivery.

The authors consider the Ventouse to be safe for mother and child. Although the instrument can effectively replace the obstetric forceps in most instances, even as a "trial tractor", it is not recommended in cases of acute foetal distress or where there is material disproportion, and routine use of the Ventouse and exclusion of obstetrical forceps is not advocated. The authors merely recommend "using it freely", and this is borne out by their figures for the year ending April, 1959, when the Ventouse was used in 6·6 per cent and forceps were used in 4·1 per cent of 1,035 deliveries. *R. W. Grayburn*

343. **The Treatment of Transverse Lie.** (Nochmals über die Behandlung der Querlage.)

By I. ZOLTÁN. *Zbl. Gynäk.*, **82**, 912–920. June 11, 1960. 2 tables. 23 refs.

The fault of treatment by version of a transverse lie is that it may correct the malpresentation but fail to deal with the predisposing or associated abnormalities which contribute to foetal risks. As a result of the more liberal use of Caesarean section the corrected foetal mortality fell from 20 per cent during the years 1947–1948 when the operation was used in 50 per cent of cases, to 2·2 per cent during the years 1949–1957 when it was used in 75·3 per cent.

After discussing the views of other workers in this field, the author concludes that external version is only rarely justified under the following conditions: there should not be any uterine inertia; it should only be used for multigravidae who have not lost any previous child; the lie should be oblique rather than transverse so that the external manipulation should be minimal; the membranes should be intact; the attempt at version should be made once only and without the use of general anaesthesia. Podalic version is used in cases of twins provided the first twin lies longitudinally; in cases of a dead or non-viable foetus; in multiparae if at the time of the examination the cervix is at least 4 fingers dilated, the membranes intact, the foetus not too large, and previous labours have been uncomplicated.

[Unfortunately the author does not give figures concerning the gross foetal mortality.] *Bruce Eton*

344. **Prevention of Abortion and Premature Labour by Suture of the Cervix.** (Verhinderung von Fehl- und Frühgeburten durch Muttermundverschluss.)

By B. SZENDI. *Zbl. Gynäk.*, **82**, 1106–1116, July 16, 1960. 19 refs. 7 illus.

The author reports the results of the Shirodkar operation carried out in 10 patients with a previous history of mid-pregnancy abortion or very premature labours. The surgical procedure was carried out without incising the anterior vaginal wall in order to avoid bleeding. It is claimed that the anatomical os can be reached without risking injury to the bladder, although it is not pushed up before the stitch is inserted. The knot is tied in front of the cervix. Adrenaline is administered in order to inhibit uterine contractions.

In 7 successful cases the cervix was sutured although uterine contractions had started. In two other cases treated in the seventh month although in early labour, the process proved to be almost irreversible in spite of adrenaline, so that the stitch had to be removed one week later and delivery took place. One other patient was admitted with uterine contractions during the 5th month. The cervix was sutured and labour pains subsided with rest and adrenaline. She was re-admitted with labour pains on two further occasions, the last time at 33 weeks when the membranes ruptured. She drained liquor for 23 days and the pregnancy had reached 36 weeks when labour became irreversible. The child delivered by Caesarean section weighed 2,100 g. and died after two days.

The author admits that the operation is more successful if carried out prophylactically before the onset of uterine contractions, as the uterus in labour is dominated by the parasympathetic. In his experience however it is often successful even in the early stages of threatened abortion, provided treatment with adrenaline forms part of the management. *Bruce Eton*

345. **Conservative Surgery for Tubal Pregnancy.** (Die konservative Operation der Tubargravidität.)

By G. SCHENK. *Zbl. Gynäk.*, **82,** 863–866, June 4, 1960. 10 refs.

The author advocates conservative surgery in cases of tubal pregnancy in women whose other Fallopian tube is absent. The affected tube is incised longitudinally and the ovum is expressed cautiously. The site of implantation is gently freed of any remaining villi and then the patency of the tube is tested by means of a sound. The incision is closed with catgut stitches turning the edges inwards in two layers. No attempt is made to achieve absolute haemostasis in the tubal wall. The surgical procedure should, if possible, avoid the fimbriated end, which is of the greatest importance for subsequent conception and transport of the ovum.

Four patients were treated in the manner described. One patient has since then had two successful uterine pregnancies, including one set of twins. A second patient had one subsequent uterine pregnancy and normal delivery. In the third patient follow-up salpingography showed normal patency of the tube. In the fourth patient subsequent salpingography showed a picture suggesting peri-tubal adhesions.

The author concludes that the risk of a further tubal pregnancy after conservative surgery may not be as great as generally accepted. For some years he has been conserving the affected tube whenever possible.

[The abstracter has recently removed a pregnant tube from a patient in whom such conservative surgery had been carried out previously elsewhere!] *Bruce Eton*

GYNAECOLOGY

DISORDERS OF FUNCTION

346. **Electromyographic Tests: A Possible Means of Controlling Clinically the Effect and Duration of Action of a Depot-Preparation of Corpus Luteum Hormone.** (Elektromyographische Testuntersuchungen. Eine Möglichkeit für die klinische Kontrolle der Wirkung und Wirkungsdauer eines Gelbkörperhormon-Depotpräparates.)

By Y. UEDA and J. OMICHI. *Zbl. Gynäk.*, **82,** 1019–1025, July 2, 1960. 7 figs. 8 refs.

Following the discovery by Kawakami (*Jap. J. Physiol.*, 1954, **4,** 274) that the abdominal muscles show a behaviour specific for pregnancy regarding the suppression of action currents when tested by electromyography, the authors carried out electromyographic studies after administration of two progestogens: progesterone and 17α Hydroxy-progesterone-17-capronate (HPC). The subjects were seven healthy male and female non-pregnant undergraduates and three women castrated by oöphorectomy.

It was found that HPC has, in common with the natural hormone, not only the ability of raising the basal temperature, but also that of inhibiting action currents normally observed in the skeletal musculature of both sexes. In the case of the synthetic depot-preparation this effect is prolonged, as are the other progestational effects of HPC. The effect is observed more readily and lasts longer in women than it does in men.

The action of HPC can, of course, not be assessed by urinary pregnanediol assays, as it is not excreted in that form. *Bruce Eton*

347. **The Treatment of Uterine Hypoplasia by Production of Pseudo-Pregnancy Using the New Progestogenic Steroids.** (Sulla terapia dell'ipoplasia uterina mediante provocazione della pseudogravidanza coi nuovi progesteroidi.)

By A. MIGLIAVACCA. *Ann. Ostet. Ginec.*, **82,** 490, May, 1960. 22 refs.

The most active of the progestin compounds so far synthesized is 6-alpha-methyl-17-alpha-hydroxy-progesterone acetate or MAP. This has been shown to induce an endocrine condition somewhat similar to the typical alterations of pregnancy. This has been used, in combination with small doses of oestrogen to produce a state of pseudo-pregnancy in cases of uterine hypoplasia with the idea that as the uterus grows in normal pregnancy so it would grow in a condition of pseudo-pregnancy.

The dosage used is so far provisional and begins with three doses of ethinyl oestradiol of 0·05 mg. with three doses of 10 mg. of MAP daily for the first week. This is gradually increased until in the fourth week the dosage of MAP is 60 mg. a day.

Basal body temperature rose from the second day and remained high until the end of treatment, falling the day after cessation of treatment.

The immediate result was an increase in the size of the uterus; the hystometric value increased by two-thirds and was sometimes doubled. The size of the uterine cavity as seen by hysterography was increased. The flexion of the body of the uterus on the cervix was diminished. The endometrium showed different changes in individual cases. These varied from hypertrophy with extreme secretory activity to a pronounced functional depression of epithelial elements. There was no sign of decidual change in the stroma. A striking effect was the increase in size of the breasts with mastodynia during the period of treatment. The patients felt well and in some libido was increased.

In two cases of hypoplasia conception occurred during treatment, while in a third conception occurred four months after the completion of treatment.

Josephine Barnes

348. **The Use of the New Progestogens in the Treatment of Functional Uterine Haemorrhage.** (I nuovi progestinici al vaglio della terapie delle anomalie mestruali in eccesso.)

By G. DELLEPIANE. *Ann. Ostet. Ginec.*, **82,** 519, May 1960. 6 figs. 14 refs.

The therapeutic effect of three of the new synthetic progestogens (6-alpha-methyl-17-alpha acetoxypro-

gesterone, 17-alpha-ethinyl-19-nortestosterone and 17-alpha-methyl-19-nortestosterone) have been tried in cases of functional uterine haemorrhage. The doses have varied between 10 and 20 mg. per day and the substances have been used both in prevention and treatment.

The production of "medical curettage" is beneficial in many cases of functional haemorrhage.

In puberty bleeding this treatment, combined with human chorionic gonadotrophin has proved very successful. In the pre-menopausal forms, differentiation between organic and functional causes is most important; histological examination of the endometrium is essential before treatment is given.

Josephine Barnes

349. **Intractable Uterine Haemorrhage Due to Abnormal Subendometrial Blood Vessels After Childbirth and Miscarriage.**

By R. SALM and P. N. SIMONS. *Brit. med. J.*, **1**, 1534–1537, May 21, 1960. 2 refs.

Two cases are described in which recurrent exsanguinating menorrhagia followed childbirth and miscarriage. Both were considered functional in origin at the onset. Conservative measures failed to prevent the severe uterine haemorrhages and finally hysterectomy was resorted to.

Detailed examination of the operation specimens revealed large thick-walled subendometrial blood vessels, probably arterial branches which had supplied the placental site and which had failed to undergo involution in the usual way during the puerperium. Erosion of these vessels during menstruation was regarded as the cause of the exceptionally severe menorrhagia.

As far as the authors are aware, the syndrome has not previously been recorded.

R. W. Grayburn

350. **Causes of Post-menopausal Bleeding.** (Sul significato clinico delle metrorragie nella menopausa.)

By G. BENZI. *Minerva ginec. (Torino)*, **12**, 371–377, Apr. 15, 1960. 5 tables. 3 figs. 72 refs.

Figures are published of 210 women aged over 48 and at least one year past the menopause, reporting for haemorrhage from the genital tract, with an analysis of the causes of the bleeding.

In 162 the cause was diagnosed as non-malignant and in only 48 was it due to neoplastic disease. In the former category the chief causes were cervical polyp and atrophic endometritis (34 cases each). In 12 cases it was withdrawal bleeding after treatment with oestrogens, a figure shared with prolapse, hyperplastic endometrium and "unknown". Of the 48 neoplastic cases, 21 were due to cancer of the body and 17 of the cervix of the uterus. The percentage due to malignant disease was much higher in the older age groups. The comparatively low incidence of neoplastic causes, said to be in agreement with figures recently published elsewhere, is attributed to a better public appreciation of the importance of the symptoms.

W. C. Spackman

351. **Abnormalities Involving the X Chromosome in Women.**

By P. A. JACOBS, D. G. HARNDEN, W. M. COURT BROWN, J. GOLDSTEIN, H. G. CLOSE, T. N. MACGREGOR, N. MACLEAN and J. A. STRONG. *Lancet*, **1**, 1213–1216, June 4, 1960. 4 tables, 2 figs. 15 refs.

The authors report 3 cases of chromosomal abnormalities involving the X chromosome. The patients, all of female phenotype, were considered to have an XXO/XO mosaic pattern, a partial deletion of one X chromosome and an XXX sex chromosomal pattern respectively. The clinical features of the patients are described and it is noteworthy that the patient with the XXX pattern did not appear to have any related physical abnormality. Unlike the other 2 patients who had primary amenorrhoea, she menstruated normally. Evidence of ovulation had not been forthcoming but the possibility exists that patients with an XXX constitution are fertile. It is recommended that routine buccal mucosal smears should be examined for sex chromatin in all unexplained cases of amenorrhoea.

[A case of fertility and oligophrenia in an apparent triplo-X female has been described since the publication of the above paper (Stewart, J. S. S., and Sanderson, A. R., *Lancet*, 1960, **2**, 21).]

J. M. Brudenell

352. **Synthetic Progestogens and Ovulation.** (Progestativi di sintesi e ovulazione.)

By F. VOZZA and F. E. MANSANI. *Ann. Ostet. Ginec.*, **82**, 463, May 1960. 21 figs. 33 refs.

The effects of high and average doses of three synthetic progestogens have been tried in mature female virgin rabbits. The three substances used were 6-alpha-methyl-17-alpha-hydroxyprogesterone, 17-alpha-ethinyl-19-nortestosterone and 17-alpha-methyl-19-nortestosterone. Observations were made on the histological changes observed in the anterior pituitary.

The most important changes noted were:

(1) Intense congestion throughout the whole genital apparatus with high or prolonged dosage.

(2) Pronounced hypertrophy of the uterus and ovary.

(3) With medium doses and with brief administration of high dosage the progestational response was incomplete, with discrepancies between the epithelial and the stromal response. With high dosage over a protracted period the progestational response in the endometrium was complete.

(4) The first two preparations produced changes in the ovarian follicles with regression of primordial follicles and follicular haemorrhages.

(5) There was an absence of gonadotrophic activity of the hypophysis in treated animals.

Josephine Barnes

353. **The Stimulation and Inhibition of Ovulation Using Steroid Hormones.** (Auslösung und Unterdrückung einer Ovulation mit Steroidhormonen.)

By P. POTS. *Geburtsh. u. Frauenheilk.*, **20**, 851–855. July 1960. 4 tables. 36 refs.

Infertile women with anovulatory cycles were treated with hormones, in an attempt to induce ovulation. A single intramuscular injection of oestrogen (5–50 mg. of oestradiol benzoate or dienoestrol diacetate) was given 1,297 times to 220 patients and ovulation occurred on 8 (0·6 per cent) occasions only. The presence or absence of ovulation was judged by the basal temperature, pregnanediol excretion, the luteinization of vaginal smears and the presence of secretory activity in the endometrium. Ovulation did not occur in 19 women who were given a prolonged course of oestrogens by mouth (280 mg. of dienoestrol diacetate spread over 8 weeks). Two hundred and twenty patients were given a total of 1,342 injections of 50–100 mg. of progesterone at intervals of 4 weeks and ovulation occurred 11 times (0·8 per cent). Although the basal temperature rose and the vaginal smear altered in response to oral treatment of 118 patients treated with ethinyl nortestosterone for 407 cycles, no definite evidence, in the form of pregnanediol excretion, was obtained to show that ovulation had occurred.

Peter J. Huntingford

354. **Is There a Stein-Leventhal Syndrome?**
By D. W. T. ROBERTS and M. HAINES. *Brit. med. J.*, 1, 1709–1711, June 4, 1960. 16 refs.

Twenty-one patients divided into 3 groups form the basis of this study. The 3 groups were (1) Typical histology+clinical syndrome of infertility, irregular periods and hirsutism. (2) Typical histology+clinical syndrome and corpus luteum. (3) Controls; patients in the same age-group seen during the same period of time but with varying indications for operation.

The findings are quite different from any reported so far, in that symptomology and histology did not necessarily go together. The ovarian histological picture was found in some patients without symptoms, and normal corpora lutea were revealed in patients who had symptoms. The appearance of the ovarian cells gave no indication of the causal condition.

The conclusion is reached that the Stein-Leventhal syndrome does not appear to be a well-defined entity. It would be more apt to refer to the condition as multiple small follicular cysts of the ovary, rather than cling to the eponymous nomenclature suggesting symptoms and signs which may not be present. If a patient is infertile and has palpably enlarged ovaries and no evidence of ovulation, there is adequate justification for the performance of wedge resection which gives her a chance of ovulating and becoming pregnant.

R. W. Grayburn

355. **Certain Characteristics of Cervical Mucus in Relation to the Menstrual Cycle.**
By C. HARVEY, R. A. LINN and M. H. JACKSON. *J. Reprod. and Fertil.*, **1**, 157–168, 1960. 1 plate. 12 figs. 12 refs.

The authors studied the consistency index of cervical mucus throughout the menstrual cycle in a series of 125 women and observations were made on the characteristics of 24 samples obtained on the day when conception was known to have occurred.

Confirmation was obtained that the consistency was lowest from the 12th to the 19th days before menstruation the values for recoil being maximal over the same interval. Spermatozoal progress and invasion were only found to be satisfactory in low consistency mucus, although there was little correlation between sperm activity and recoil. No peak concentration of glucose was demonstrated, although this may have been due to the variable sensitivity of the material used for testing.

In an analysis of the characteristics of cervical mucus in those cases where pregnancy was known to have resulted, it was concluded that the most valuable and practical aids to pinpointing ovulation were the basal temperature charts followed by the appearance of the mucus and the character of the thread. Cycle days 12 and 13 stood out as the best on which to carry out insemination or to advise a couple to have coitus.

A. E. R. Buckle

356. **A New Fertility Testing Tape.**
By J. B. DOYLE, F. J. EWERS and D. SAPIT. *J. Amer. med. Ass.*, **172**, 1744–1750, Apr. 16, 1960. 5 figs. 11 refs.

During the pre-ovulatory phase of the menstrual cycle the cervical mucosa and the endometrium secrete glycogen and other polysaccharides to furnish an extrinsic source of energy for the anaerobic metabolism of the sperm and the ovum. From the Fertility Clinic, St. Elizabeth's Hospital, the authors describe a new test tape impregnated with glucose oxidase. When this comes into contact with the cervical mucous cascade it catalyzes the oxidation of glucose to gluconic acid, and the reactions following change the tape's pink colour to blue. This is considered to be an improvement upon tapes containing orthotolidine because the chemical similarity of the latter to benzidine is occasionally responsible for false positive results.

The technique is described in detail and involves the use of a special introducer like a plastic syringe. The deep blue colour change usually occurs synchronously with ovulation. It is suggested that the glucose present in the cervical mucous cascade may be partly from aspirated liquor folliculi and confirmation of this was obtained from 35 patients whose positive glucose reactions preceded abdominal operation. All of these patients showed ruptured Graafian follicles or early active corpora lutea. Cul-de-sac puncture also showed the presence of glucose in the pelvic pool and all these changes are demonstrated by colour photographs. With this new evidence of ovulation natural child spacing by positive or negative family planning can be carried out inexpensively and without moral scruples.

D. W. James

357. **Semen Transport Inside the Female Genital Tract.** (Der Samentransport in das innere Genitale der Frau.)
By J. TRAPL. *Arch. Gynäk.*, **192**, 668–690. 1960. 3 figs. 79 refs.

After an extensive survey of the literature on the subject the author discusses his own views based on experimental evidence. There are two opposing schools among the workers in this field. Whereas one group supports the theory of active ascension of spermatozoa from the posterior fornix to the ovary, the other group maintains that semen is moved passively by the muscular action of the inner organs. The former theory is supported by the fact that pregnancy may occur with intact hymen, during anaesthesia, in a fainting fit, after "coitus ante portas", etc. The changes occurring in the physical properties of cervical mucus around ovulation time also favour the "active movement" theory. The other school maintains that during the act of coitus a negative pressure is created in the vagina during which the cervical mucus is sucked into the uterus. Live spermatozoa have been found in utero-abdominal fistulae of experimental animals as soon as 25 seconds after intercourse.

The author's own experiments were carried out on laboratory animals and female patients. Rabbit does were stimulated by pregnyl and oestrogen 12 hours before the introduction of 4 ml. of contrast medium intravaginally. The animals were subsequently mated. Four hours later contraction of the vaginal wall occurred and the contrast medium moved upwards towards the cervix and could be followed radiologically into one uterine horn. Contrast medium was injected into 3 women (sterility patients) and followed by means of a fluorescent screen. One single peristaltic wave transported the bulk of the injected material from the neck of the womb into the tubes. Other experiments concerned the transport of lifeless particles. Suppositories containing Indian ink were introduced into the vaginae of rats and guinea-pigs in pro-oestrus and the animals were subsequently mated. Twelve hours later laparotomy was performed and spermatozoa and Indian ink particles were recovered from the uterine horns of each animal. One female patient in mid-cycle was asked to introduce a similar suppository vaginally and to have intercourse by condom half an hour later. She underwent a hysterectomy operation for fibroids on the following morning. Indian ink stained particles were found in the cervical mucus, the ampullary ends and the walls of the tubes and in the Pouch of Douglas.

The author concludes from these experiments that the transport of semen is predominantly due to muscular contractions, and that sperm motility plays only a minor role in the approach of the spermatozoon to the ovum.

Erica Wachtel

358. **The Speed of Human Spermatozoa and the Effect On It of Various Diluents, with Some Preliminary Observations on Clinical Material.**

By C. HARVEY. *J. Reprod. and Fertil.*, **1**, 84–95, 1960. 2 tables. 7 figs. 13 refs.

It is pointed out that "quality" of movement is probably at least as important as percentage motility as a measure of potential fertility of semen, factors such as temperature and long incubation in diluting media affecting the rate of movement of spermatozoa. A method for the estimation of the speed of movement of spermatozoa involving the suspension of a fixed quantity of semen with a fixed quantity of diluent and the tracking of the path of individual spermatozoa over a grid counting slide is described.

The initial average speed in undiluted semen was from 30–68 μ per second and a reduction of 10–20 per cent followed when the sperms were suspended in plasma, normal saline or glucose-phosphate solution. Suspension in a slightly acid medium also resulted in a fall in speed.

The relation of sperm speed to potential fertility was estimated by observations on sperms from the semen of husbands of patients attending the sub-fertility clinic but no reliable conclusion was reached.

By estimation of the speed of movement through cervical mucus, confirmation of the fact that sperms can reach the oviducts within 30 minutes of insemination was obtained.

A. E. R. Buckle

359. **Nuclear Morphology of Human Spermatozoa.**

By L. B. SHETTLES. *Obstet. and Gynec.*, **16**, 10–14, July 1960. 7 figs. 4 refs.

Using a phase-contrast microscope and dried unstained smears of human spermatozoa, the author has examined and photographed the head morphology of the spermatozoa. Two distinct types of head are seen which differ in head and nuclear size, shape, diffraction of light and chromosomal pattern. The relative sizes and shapes of the most centrally located chromosomes indicate that the smaller-headed spermatozoa contain the Y chromosome and the larger the X. With the 2 distinct types now recognizable, the efficacy of attempts to separate them artificially can be studied.

J. G. Dumoulin

360. **Varicocele Ligation with Improved Fertility.**

By L. S. SCOTT. *J. Reprod. and Fertil.*, **1**, 45–51, 1960. 6 tables. 1 fig. 6 refs.

The author describes the effects on fertility of 55 cases of varicocele ligation personally operated upon and clinically assessed. Four sub-fertile men without varicocele voluntarily consented to operation and acted as "controls".

Operation consisted of ligation and division of the single vessel, formed by union of the pampiniform veins, below the deep inguinal ring, access being obtained through the usual inguinal hernia exposure.

Assuming a sperm count of 20 million per ml. and an active motility of 50 per cent at 4 hours as being a "fertile" specimen, it was found that, excluding right-sided varicoceles and cases with other complicating factors (such as maldescent of the opposite testis with hypospermatogenesis of the testis on the side of the varicocele), a return to "fertility" was obtained in some 70 per cent of cases within 6 months of operation.

Virtual azoospermia was not a complete contra-indication to operation but good results cannot be anticipated, as many cases show histological evidence of irreversible damage to the germinal epithelium. Operation

in complete necrospermia associated with a normal sperm count led to an excellent response in 75 per cent of cases and low grade motility associated with an adequate sperm count was felt to be one of the strongest indications for varicocele ligation.

No change in fertility followed ligation of the spermatic vein in the absence of varicocele, nor ligation of right-sided varicoceles.

A significant rise in pregnancy rate also followed, in successful cases, within a few months of operation.

A. E. R. Buckle

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

361. **Relation Between Pregnancy and Carcinoma of the Cervix.** (Beiträge zum Zusammenhang zwischen Schwangerschaft und Portiokarzinom.)

By G. ANTAL and K. ABRAHAM. *Zbl. Gynäk.*, **82**, 1036–1043, July 2, 1960. 6 figs. 10 refs.

The modern aim of detecting carcinoma of the cervix in its earliest possible stages has led some zealous investigators to examine the cervix in pregnancy in view of the known relationship between parity and the incidence of the cancer. With colposcopic examination and cervical biopsy in 100 patients atypical epithelium was seen 7 times, with occasional findings suggestive of a carcinoma *in situ*. The authors deliberately withheld radical treatment but limited themselves to careful observation and follow-up examinations. In the course of the subsequent 10 months no case was found in which changes of definitely malignant character persisted. The biopsies taken after these pregnancies showed normal epithelium, and the atypical epithelium previously noted during colposcopy underwent regression.

The authors therefore issue a warning against radical treatment if such histologically suspicious findings are made during pregnancy, but they emphasize that a conservative attitude is only justified, if the medical attendant is prepared to continue supervision of the patient, if necessary for several years.

Bruce Eton

OPERATIONS

362. **Normal and Pathological Changes in the Electrolytes Following Gynaecological Operations.** (Normale und pathologische Veränderungen des Elektrolythaushaltes nach gynäkoligischen Operationen.)

By V. FRIEDBERG and E. HELLMICH. *Geburtsh. u. Frauenheilk.*, **20**, 809–827, July 1960. 7 figs. 53 refs.

In 58 patients, who were subjected to gynaecological operations of graded severity, estimations of the electrolyte content of blood and urine were made before and after operation. Reduction in urinary output was short-lived and confined to the few hours immediately after the operation. Potassium excretion was greatly increased during the first post-operative day. There was a significant retention of sodium from the 2nd–5th days following the operation. Post-operative sodium and water retention did not appear to be related to the severity of the operation, as long as the blood volume was adequately maintained, and as long as this was achieved by means of blood, rather than any other intravenous fluid. The mechanism of these changes remains doubtful, because the only alteration in the output of antidiuretic hormone was a brief rise on the first day; and also because aldosterone output was seldom increased unless there had been a reduction of the blood volume sufficient to cause severe shock.

Peter J. Huntingford

363. **Electronic Flash Photography During Peritoneoscopy.** (La photographie au flash électronique au cours des coelioscopies.)

By J. THOYER-ROZAT. *Gynéc. et Obstét.*, **59**, 71–73, Jan.–Mar. 1960.

This is a short paper with six beautiful colour plates showing photographs taken of:

(1) Healthy tubes, (2) subserous fibroid, (3) tubular pregnancy with haematocele, (4) torsion of the tube, (5) double hydrosalpinx and (6) salpingo-oöphoritis, through a peritoneoscope.

Elliot E. Philipp

364. **Isthmial Incompetence. Manometric Hysterography with a Balloon.** (Béances isthmiques. Hystérographies manométriques avec ballonnet.)

By E. HERVET, R. TROCELLIER and C. CHICHA. *Gynéc. et Obstét.*, **59**, 88–100, Jan.–Mar. 1960. 18 figs.

This is a preliminary report on the use of an instrument which incorporates a simple balloon that can be introduced into the uterus and connected to a manometer.

The machine was described in a previous abstract (*J. Obstet. Gynaec. Brit. Emp.*, 1960, **67**, 700).

With the machine they have investigated:

(1) A control series of women in two phases of the menstrual cycle and in the immediate post-partum phase. These women had no previous history suggestive of incompetence.

(2) A series of women with typical isthmial incompetence.

(3) A series of women whose case histories suggest that such incompetence is likely.

They now specify details of the normal:

(1) The normal diameter of the isthmus is between 5 and 8 mm.

(2) The diameter varies according to the phase of the menstrual cycle. It is larger in the first half and smaller in the second. It is relatively hypertonic as compared with the body of the uterus in the first half of the cycle and relaxed in the second half.

(3) There is flattening-out of the curve of pressure in the second half.

They demonstrate the various pressures obtained according to the amount of radio-opaque substance instilled into the balloon. It varies from 60 mm. Hg with 4 ml. of fluid to 100 Hg with 10 ml. of fluid. Very cleverly, they have superimposed various plates on one

another to show that the diameter does not vary in spite of the quantity of fluid injected and the pressure exerted.

In women with a known incompetence, the diameter has been shown to be 12 to 14 mm.

In "suspect" incompetence the diameters are on an average 9 mm. in the first half of the cycle and 7 mm. in the second half.

[Insufficient pressure readings have yet been taken in cases of incompetent cervix to be of value.]

Elliot E. Philipp

365. **Resection of the Body of the Uterus.**

By N. O. KARLEN. *Acta obstet. gynec. scand.*, **39**, 185–193. 1960. 2 figs. 27 refs.

The author recommends—for psychological reasons—resection of the body of the uterus with preservation of part of the functioning endometrium in preference to supra-vaginal hysterectomy, for patients under the age of 45, particularly in cases of fundal sub-mucous myomata ("which can be lifted from the remaining uterine cavity like an egg from an egg-cup") of stubborn recurrent dysfunctional bleeding, and occasionally of severe dysmenorrhoea.

Out of 100 women who had undergone this operation at Norrköping (Sweden) Hospital, 90 were followed up. In 68 patients menstruation had continued for from one to over 10 years after the operation, depending on their age at the time of the resection of the uterine body. In 22 patients the operation was followed by amenorrhoea; nine of them were of menopausal age, and only 8 of them had been eumenorrhoeic before the operation.

The author concludes that these results corroborate the view that ovarian function persists after hysterectomy.

N. Alders

366. **Combined Rectal and Uterine Prolapse.**

By R. V. BHATT. *J. Obstet. Gynaec. India*, **10**, 476–484, June 1960. 3 figs. 30 refs.

Five cases are reported of the unusual combination of combined prolapse of the rectum and of the uterus. Rectal prolapse is more common in the female than in the male but childbirth is not thought to be an aetiological factor in its causation, as it appears to be as common in nulliparous as in parous women. In India, however, rectal prolapse is more common in men, and the author thinks that the association of rectal and uterine prolapse in women is fortuitous. As rectal prolapse occurs in late rather than in early life, it may be that Indian women seldom reach the age group in which it occurs.

Three types of case are recognized. In the first type, uterine prolapse is the main feature, and rectal prolapse is minimal. Following colporrhaphies or a vaginal hysterectomy, the rectal prolapse is injected with sclerosing solution or is excised.

There may be complete rectal prolapse, with a lesser degree of cystocele and rectocele, when colporrhaphy may be followed by anterior resection of the rectum or by recto-sigmoidectomy. In both types the vaginal and rectal procedures are carried out independently.

When there is complete prolapse of both uterus and rectum, it is recommended that both conditions are operated on concurrently, as in Dickson Wright's operation for the elderly patients in whom it occurs. He introduces a figure-of-eight silver wire loop encircling both anal and vaginal orifices and crossing in the perineal area. Or Le Fort's operation may be followed by Thiersch's operation to tighten the anal sphincter.

John McKiddie

367. **Our Experiences with the Marshall-Marchetti-Krantz Operation.** (Über unsere Erfahrungen mit der Operation nach Marshall-Marchetti-Krantz.)

By G. MOLNÁR and L. KAPU. *Zbl. Gynäk.*, **82**, 1147–1151, July 23, 1960. 2 figs. 14 refs.

The authors review the results of urethro-vesico-fixation in 58 patients suffering from stress incontinence (SI). The cases were divided into 3 categories:

(1) 24 patients previously treated for SI by means of vaginal plastic procedures;
(2) 18 patients with SI without utero-vaginal prolapse;
(3) 16 patients who had SI and required laparotomy for some other indication.

In all cases the incontinence was investigated prior to operation by examination of the urine, cystoscopy, sphincterometry and urethro-cystography. The surgical procedure consisted in fixing the urethra and the bladder neck to the periosteum behind the symphysis with 6–8 silk stitches, except for the last two which were passed through the rectus sheath.

Fifty-four patients reported for follow-up examination between 3 and 12 months after operation. The functional result was excellent in 38, fair in 12, and poor in 4. The result was regarded as successful in 50 out of the 54 patients seen (92·5 per cent). All four failures occurred in patients belonging to the first category.

Classification of the SI before operation according to 3 degrees of severity showed that all patients who had suffered from the worst degree of SI were cured. Three of the failures occurred in patients with the mildest degree of SI and the 4th failure in a patient belonging to the intermediate group.

Bruce Eton

368. **Stress Incontinence of Urine. A Survey of 34 Cases Treated by the Millin I Sling Operation.**

By C. KENNEDY. *Brit. med. J.*, **2**, 263–267. July 23, 1960. 28 refs.

Stress incontinence is associated with utero-vaginal prolapse in 40–50 per cent of cases. In many cases the symptom persists following a plastic repair operation. Nevertheless in the parous patient with laxity of the vaginal walls and stress incontinence, a vaginal plastic repair operation should always be done in the first place. If this has been done and stress incontinence still exists without laxity then there is an important place for some form of sling operation. In the case of a nullipara who suffers from stress incontinence, and in whom there is no laxity, a sling operation may be undertaken as a primary procedure provided that bladder and neurological

investigations reveal no lesion to account for the symptom.

The author records his experience of 34 cases of stress incontinence treated by the Millin I operation. Thirty-one had had one or more previous plastic repair operations; in three the operation was the first method of treatment. His cure rate was 87·5 per cent. He suggests that though the operation may sometimes be technically difficult, though there is a high percentage of temporary bladder trauma (52·9 per cent in this series) and though the immediate post-operative nursing is exacting and convalescence a little prolonged, sling operations might be practised more often with advantage.

R. W. Grayburn

UROLOGY

369. **Modern Views on Female Micturition with a Note on the Incidence of Orthostatic Incontinence of Urine.** (Conceptions actuelles sur la miction de la femme. Incidences sur l'incontinence orthostatique d'urine.)

By F. LEPAGE and H. DE TOURRIS. *Gynéc. et Obstét.*, **59**, 57–70, Jan.–Mar. 1960. 7 figs. 99 refs.

In this paper the authors review the classical idea of the control of micturition. It used to be considered that there was a smooth muscle sphincter continuous with the bladder detrusor muscle in the upper part of the urethra, and a striped muscle sphincter situated lower down; and that the first muscle is an involuntary muscle with sympathetic innervation and the second a voluntary muscle supplied by the internal pudendal nerve. They throw doubt on the existence of a smooth muscle sphincter in the upper part of the urethra, and they bring anatomical, cystoscopic, radiological, radiocinematographic, manometric and sphincterometric studies to show that there is only one sphincter and that that is the striped muscle sphincter.

They say that since there is no smooth muscle sphincter in the upper part of the urethra, what happens at the onset of micturition is that the upper part of the urethra becomes a funnel continuous with the bladder, the whole resembling a pear with its lowest point situated at the striped muscle. The funnel opens by contraction of the detrusor muscle and it closes through turgidity of the trigone, and folding over of tissues at the upper end of the urethra.

The illustrations are drawings to support their theory and to show why and how operations like the Perrin-Marchia, the Marion and the sling procedures work.

Elliot E. Philipp

370. **The Female Prostate. Bladder Neck Obstruction in Women.**

By T. MOORE. *Lancet*, **1**, 1305–1309, June 18, 1960. 6 figs. 6 refs.

The author describes 33 cases of bladder neck obstruction in women; he draws attention to the presence of many glands surrounding the female urethra and representing the homologue of the male prostate. Hypertrophy of these glands may occur in the region of the bladder neck and with squamous metaplasia of its epithelial lining, infiltration with inflammatory cells, oedema or fibrosis leads to interference with micturition. Most of the patients fell into the normal "prostatic" age group and complained of difficulty in starting micturition. With increasing obstruction, residual urine gave rise to frequency of micturition. Occasionally acute retention occurred particularly when the patient was confined to bed. Long-standing obstruction led to impaired renal function and even uraemia in some cases.

The condition was diagnosed by means of cystourethroscopy, a prominent lip being seen in the posterior quadrant of the bladder neck. The overlying mucosa was frequently swollen, oedematous and polypoid, the result of long-standing inflammatory changes in the urethra. Movement of the bladder neck during attempted micturition was seen to be more limited than normal. Relief of the obstruction was brought about in 29 of the 33 cases by means of a small transurethral resection of the bladder neck, preceded in those cases of severe renal dysfunction by a period of urethral catheter drainage. The author feels strongly that obstructive symptoms are never the result of an uncomplicated cystocele and deprecates the use of colporrhaphy which by reason of the post-operative para-urethral fibrosis makes the patients' symptoms worse rather than better.

Of the patients treated by bladder neck resection the result to the patient was assessed as being good in 26 cases. A few patients required more than one operation but the majority were cured at the first attempt.

J. M. Brudenell

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Each sentence should have its proper components thus:

"*Progress:* The patient continued to improve," NOT "*Progress:* Went downhill."

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Dates should be given as 10th May, 1946, and *not* 10.V.46. Numbers should be in the form of numerals and not words except when beginning a sentence, thus "Fifteen patients out of a total of 60 exhibited," etc. The official rather than the proprietary names of drugs must be used. The Journal convention is gr. for grains; g. for grammes; Kg.; ml. (*not* c.c. or c.cm.); mg.; pounds (*not* lb.); ounces (*not* oz.), etc., and wherever suitable the metric equivalent of an English measure should be given, for example, when recording pelvic measurements, size and weight of babies, tumours, etc.

When comparable figures are given, either the English or the metric mode must be followed, thus: the excretion of urine/24 hours should be shown in ml. (and not ounces) when the urinary or blood-urea is given in g./100 ml.

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Brown, H. E., and Jones, B. K. (1943): *J. Obstet. Gynaec. Brit. Emp.*, **2**, 128.

Sampson, P. (1940): *Obstetrics for Midwives*. 2nd edition. Fraser, London. p. 9.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

AT the meeting of Council held in the College on Saturday, 26th November, 1960, with the President, Mr. A. C. H. Bell, in the Chair, the following was appointed to give the William Blair-Bell Memorial Lecture in 1961: Professor Derk Crichton, of Durban, South Africa. The William Meredith Fletcher Shaw Memorial Lecture will be given by Professor C. H. G. Macafee of Belfast.

Mr. Douglas Miller was appointed the first J. Y. Simpson Orator. The Endowment of this oration was made by Mr. V. B. Green-Armytage, a past Vice-President of the College. The President formally acknowledged the acceptance of this generous gift at the Scientific Meeting at the Royal College on 14th July. It takes the form of funds to produce an honorarium of fifty pounds each year to be used:

> "to provide for an annual oration to be known as the 'J. Y. Simpson Oration' to be given by an Honorary Fellow or Fellow of the College on the invitation of the President and Council.
>
> "The oration is to be on any approved aspect of Gynaecology and/or Obstetrics and contain in its theme and substance reference to the *man* J. Y. Simpson; for instance it could entertain in its title such a word as adventure or research or endeavour or courage or intuition or change or any other word to interest and inspire."

The Edgar-Gentilli Prize for 1961 has been awarded to Dr. J. S. Scott of Liverpool. Mr. H. H. Francis of Liverpool was appointed Bernhard Baron Travelling Scholar for 1961 to visit the United States. Dr. Bruce Eton of Cambridge was appointed Green-Armytage Short-term Travelling Scholar for 1960 to visit Vienna, and Wing-Commander G. A. Humphreys was appointed Green-Armytage Short-term Travelling Scholar for 1961, to visit Paris.

The following were admitted to the **Membership:**

Mavis Fay Anderson.
Frans Willem Van der Westhuizen.

The following have been awarded the **Diploma in Obstetrics:**

Robert Abendstern.
Edmund Ian Adam.
Ezekiel Adewumi Bolaji Adenuga.
Joseph Bandele Akingba.
John Muir Allan.
James Gourley Allardice.
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THE ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

SCIENTIFIC MEETING

PRELIMINARY NOTICE

A WHOLE-DAY Meeting, open to all practitioners interested, will take place on Friday, 24th March, 1961
Subject: "The Recognition and Treatment of Foetal Abnormality."

Opening Speakers:

Professor Thomas McKeown (Genetic Aspects).
Dr. A. E. Claireaux (Morbid Anatomy).
Dr. A. C. Stevenson (Medical Research Council).
Dr. J. P. M. Tizard (Reader, Institute of Child Health, London University).
Professor A. W. Wilkinson (Nuffield Professor of Paediatric Surgery, Institute of Child Health, University of London).

A discussion will follow.

Registration fee (to include buffet lunch), £1. Form for Registration to be obtained from the Secretary, Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent's Park, London, N.W.1.

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